A COMPARATIVE STUDY OF ESTIMATION OF LIPOPROTEIN (a) AND LIPID PROFILE IN ISCHEMIC CEREBROVASCULAR DISEASE IN PATIENTS AND MATCHED CONTROLS

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BRANCH I

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CERTIFICATE

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY OF ESTIMATION OF LIPOPROTEIN (a) AND LIPID PROFILE IN ISCHEMIC CEREBROVASCULAR DISEASE IN PATIENTS AND MATCHED CONTROLS"** is a bonafide work done by **Dr. DANTE RUSKIN** in **M.D BRANCH I GENERAL MEDICINE** at Government Mohan Kumaramangalam Medical College Hospital, Salem-636030, to be submitted to The Tamil Nadu Dr.M.G.R Medical University, in partial fulfillment of the University Rules and Regulation for the award of M.D BRANCH I GENERAL MEDICINE, under my supervision and guidance, during the academic period from May 2009 to April 2012.

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DECLARATION

I solemnly declare that this dissertation **"A COMPARATIVE STUDY OF ESTIMATION OF LIPOPROTEIN (a) AND LIPID PROFILE IN ISCHEMIC CEREBROVASCULAR DISEASE IN PATIENTS AND MATCHED CONTROLS"** was prepared by me at Government Mohan Kumaramangalam Medical College and Hospital, Salem-636030 under the guidance and supervision of **Dr.R.ANBALAGAN M.D.,** Professor and HOD of General Medicine, Govt. Mohan Kumaramangalam Medical College and Hospital Salem.

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DR. DANTE RUSKIN

LIST OF ABBREVIATIONS

AF	Atrial Fibrillation
CETP	Cholesteryl Ester Transfer Protein
CNS	Central Nervous System
CVA	Cerebrovascular Accident
DM	Diabetes Mellitus
FBS	Fasting Blood Sugar
HDL	High Density Lipoprotein
HMG-Co A	Hydroxy Methyl Glutaryl Co A
HRT	Hormone Replacement Therapy
HTN	Hypertension
IDL	Intermediate Density Lipoprotein
IHD	Ischemic Heart Disease
LCAT	Lecithin Cholesterol Acyl Transferase
LDL	Low Density Lipoprotein
Lp (a)	Lipoprotein (a)
MSF	Macrophage Stimulating Factor
PAI -1	Plasminogen Activator Inhibitor
PDGF	Platelet Derived Growth Factor
RIND	Reversible Ischemic Neurological Deficit
TC	Total cholesterol
TG	Triglycerides
TGF	Transforming Growth Factor
TIA	Transient Ischemic Attack
VLDL	Very Low Density Lipoprotein

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ABSTRACT

BACKGROUND

While Blood lipids and lipoproteins are strongly related to coronary atherosclerosis, their association with cerebrovascular atherosclerosis is less clear. Lipoprotein (a) is considered as an independent risk factor for atherosclerosis. Due to distinctive structural homology with plasminogen, it interferes with function of plasminogen thus increasing thrombotic risks. Serum lipoprotein (a) levels are genetically determined and remain almost continual throughout life being minimally affected by gender, nutrition, age, environmental factors and drugs.

Hence the present study was undertaken to estimate the serum lipoprotein (a) levels and lipid profile in ischemic cerebrovascular disease and to compare the same with matched controls.

AIM OF THE STUDY

The relation between serum lipids and ischaemic stroke remains controversial. Studies of lipid related risk factors in cerebrovascular disease have differed significantly in their findings and also in their definition of the cerebrovascular end points. Serum lipids are thought to influence the pathogenesis of stroke through an atherosclerosis mechanism. Stroke in young patients have been shown to be most commonly related to non-atherosclerotic reasons.

The aim of the study was to compare serum lipoprotein (a) level and lipid profile in ischaemic cerebrovascular disease patients and matched controls of the same age group and to find the association between lipoprotein (a) levels and lipid profile in ischaemic cerebrovascular disease.

OBJECTIVE OF THE STUDY

The study was done to find the association between lipoprotein (a) levels and lipid profile in ischaemic cerebrovascular disease.

METHODS

In this study, a total 80 subjects were included, who were divided into two groups, 40 patients with history and clinical features suggestive of ischemic stroke and confirmed by CT scan and 40 controls with no clinical history or CT scan features suggestive of recent or old ischaemic stroke. All subjects underwent a detailed evaluation for hypertension, diabetes mellitus, smoking, lipid profile and lipoprotein (a). All ischaemic stroke patients underwent a thorough evaluation for the presence of cardiac disease, by means of an ECG and 2-D ECHO.

RESULTS

Ischaemic stroke patients had higher levels of lipoprotein (a). Patients of ischemic stroke aged less than 60 years with ischemic stroke had significantly elevated lipoprotein (a). Ischaemic stroke patients with normal triglycerides and

normal total cholesterol were found to have significantly elevated lipoprotein (a) when compared to controls. However, the association of plasma lipid concentrations in ischemic stroke patients was found to be statistically insignificant in this study.

CONCLUSION

Lipoprotein (a) is an independent marker for ischemic stroke and is significantly raised in ischemic stroke patients especially in patients aged less than 60 years and in patients with normal cholesterol and triglyceride levels.

KEYWORDS

Lipoprotein (a); Ischaemic stroke; Cholesterol; Epidemiology

INTRODUCTION

Cerebrovascular disease has been shown to be one of the frequent causes of long term severe disability[1] and mortality. In 2001, WHO estimated that cerebrovascular disease accounted for 5.5 million deaths worldwide, equivalent to 9.6 % of all deaths.[2] Two-thirds of these deaths occurred in people living in developing countries. Stroke had been estimated to cause more than 4 million deaths in 1990, 75% of them in developing countries.[3] Hyperlipidemia has been established to be a risk factor for ischemic heart disease (IHD) [4]. The important role of lipids in the prevention of cerebrovascular disease has been but a new discovery.

Serum lipoprotein (a) [Lp (a)] levels are genetically determined and considered to be an independent risk factor for atherosclerosis.[5] Due to distinctive structural homology with plasminogen, it interferes with function of plasminogen thus increasing thrombotic risks.

Numerous studies have evaluated the association between Lp (a) and ischaemic (thrombotic) stroke. A few studies among the many provide inconsistent findings regarding Lp (a) as a predictor of ischemic stroke. Therefore, this study was undertaken to compare

serum lipoprotein (a) and lipid profile in ischaemic cerebrovascular disease patients and matched controls.

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The relation between serum lipids and ischaemic stroke remains controversial. Studies of lipid related risk factors in cerebrovascular disease have differed significantly in their findings and also in their definition of the cerebrovascular end points. Serum lipids are thought to influence the pathogenesis of stroke through an atherosclerosis mechanism. Stroke in young patients have been shown to be most commonly related to non-atherosclerotic reasons.

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REVIEW OF LITERATURE

HISTORY OF LIPOPROTEIN

- 1929: Michel Macheboeuf, reported the isolation from horse serum of a stable, water-soluble lipoprotein.
- 1941: Lipoproteins are separated electrophoretically by Blix et al
- 1947: Pederson was able to flotate a b-lipoprotein in the ultracentrifuge at the density of 45% saturated magnesium sulfate.
- 1949: Gofman from the University of California at Berkeley proposed a new method for the quantitative measurement of serum lipoproteins
- 1950: Gofman was then able to associate certain lipoprotein fractions with atherosclerosis and xanthomatosis.
- 1963: Ka¨re Berg discovered lipoprotein, Lp(a) in Norway in a immunochemical study.
- 1967: Fredrickson made attempts to identify the protein components (apopeptides) of the major lipoproteins.
- 1970: Fredrickson cleared that there were four families of peptides associated with the major lipoproteins.
- 1976: Jackson discovered that the A-apopeptides were associated primarily with the a-lipoproteins (HDL).

DEFINITIONS AND CLASSIFICATIONS

Stroke

A stroke or cerebrovascular disease, is the rapidly evolving loss of brain function(s) due to disturbance in the blood supply to the brain.[6]

Ischemic Stroke

In an ischemic stroke, blood supply to some parts of the brain is decreased, leading to dysfunction of the brain tissue in that area. [7] Ischemic stroke accounts for over 80% of all cases of stroke. There are four main causes for Ischemic stroke are as follows: (1) Embolism (2) Thrombosis (3) Systemic hypo perfusion and (4) Venous thrombosis.

Hemorrhagic Stroke

Intracranial hemorrhage is the accumulation of blood anywhere within the skull vault that disrupts the blood supply and chemical balance of neurons. This may be intra-axial or extra-axial. Intra-axial hemorrhage includes intraparenchymal or intraventricular forms.[8]

Transient ischemic attack (TIA)

TIA is a transient episode of neurologic dysfunction caused by ischemia – focal brain, spinal cord or retinal - without acute infarction.[9] TIAs share the same underlying etiology as strokes; a disruption of cerebral blood flow. But unlike a stroke, the symptoms of a TIA can resolve within a few minutes or 24 hours. Brain injury may occur in a TIA lasting only few minutes. The occurrence of a TIA is a risk factor for eventually having a stroke or a silent stroke.[10]

Reversible Ischemic Neurological deficit (RIND)

A cerebral infarct that lasts longer than 24 hours but less than 3 weeks is called a reversible ischemic neurologic deficit or RIND.[11] However, RIND symptoms are transitory, happening when blood flow to the brain is restricted temporarily. No permanent brain damage occurs, but RIND further increase the risk of developing a stroke.[11]

Stroke in evolution

Stroke-in-evolution is in fact a constellation of situations including various causes (lacunar, large infarcts, hemorrhages, and distal fields infarcts), various types of evolution and numerous pathophysiological mechanisms.[12] It is a progressive neurological

deficit over a few hours to days. The number of well-studied clinical cases in the literature is astoundingly small.

Completed stroke

A completed stroke is initiated by irreversible brain injury due to the interruption of blood flow.[13] It is rapid in onset with persistent neurological deficit with a temporal frame of 96 hours.[14]

EPIDEMIOLOGY

Reliable morbidity and mortality estimates for stroke in India are inadequate.[15] In India, the Council for Medical Research estimated that mortality due to strokes increased by 8% between 1998-2004.[16]

The Indian National Commission on Macro – economic and Health has estimated that the number of strokes will increase from 1,081,480 in 2000 to 1,667,372 in 2015.[17]

Prevalence/incidence of stroke in India

Prevalence data for stroke are inadequate and are confined to studies that suffer from frequent bias, small and variable sample sizes, and inconsistent diagnostic criteria. The crude prevalence rate for India varies widely according to region.[18] (Fig 1,2)

Stroke increases with age: individual Indian studies have assessed that the occurrence rates increases from 21/100,000 for the 20-40 age group to 625/100,000 in the 60+ year age group. Similarly, the incidence rates increase from 27-34/100,000 in the 35-44 age groups to 822-1116/100,000 in the 75+ age group.[19] However in

India, the prevalence of stroke in younger individuals is high (18-32% of all stoke cases) compared with high-income countries.

Table 1: Death from cerebrovascular disease in India, China and established market economies (EME) in millions

1990			2000			2010			2020		
India	China	EME	India	China	EME	India	China	EME	India	China	EME
0.45	1.27	0.79	0.6	1.65	0.87	0.75	1.91	0.88	0.95	2.29	0.91

Stroke prevalence studies in India

The crude prevalence rate appears to be higher in urban compared to rural populations. The Parsi population in Mumbai appears particularly at risk, compared with the other Indian population.[20]

The overall age adjusted prevalence rate for stroke is estimated to lie between 84-262/100,000 in rural and between 334-424/100,000 in urban areas.

Table 2: Stroke prevalence studies in India

First Author	Year	Location	Sample size	Crude prevalence per 100,000	Age-adjusted prevalence per 100,000
Urban					
Dalal PM	1997	Mumbai	145456	220	–
Banerjee TK	2001	Kolkata	50291	147	334
Gourie-Devi M	2004	Bangalore	51502	136	–
Rural					
Das SK	1996	West Bengal	37286	126	–
Saha SP	2003	West Bengal	20842	147	–
Gourie-Devi M	2004	Karnataka	51055	165	262

Figure 1: Crude prevalence rates for stroke in rural India 1970-2004

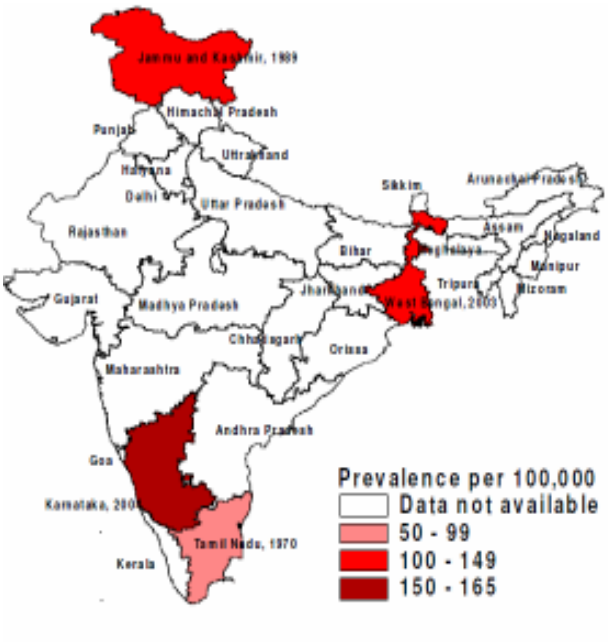
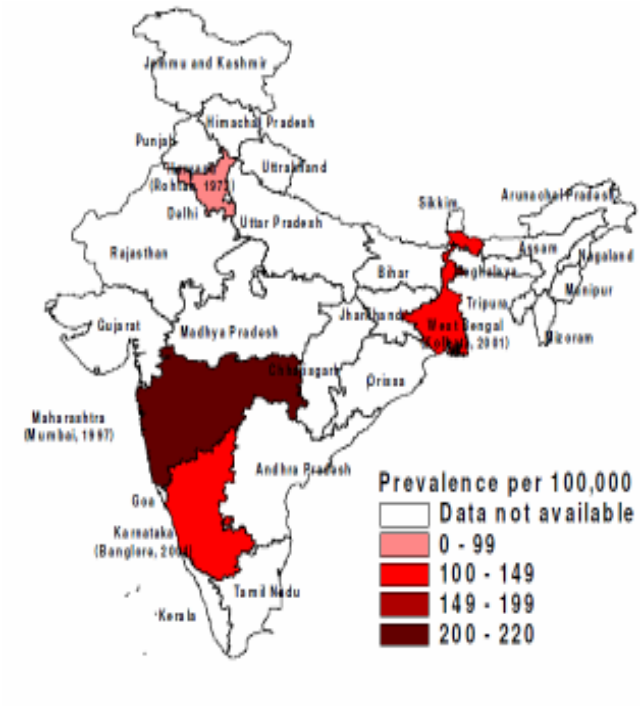


Figure 2: Crude prevalence rates for stroke in urban India 1973-2004



Annual incidence rates for stroke in India

While discrete studies have reported varying annual incidence rates for stroke, the Global Burden of Disease Study estimated a population-based annual stroke incidence of India to be 89/100,000 in 2005, which is projected to increase to 91/100,000 in 2015 and to 98/100,000 by 2030.[17]

Table 3: Annual incidence rates for stroke in India

First author	Year	Location	Sample size	Annual incidence per 100,000	Age-adjusted annual incidence per 100,000
Urban					
Banerjee TK	2001	Kolkata	50291	36	105
Dalal PM	2005	Mumbai	56861	145	152
Sridharan	2009	Trivandrum	741000	116	135
Rural					
Abraham J	1970	Tamil Nadu	258576	13	-
Sridharan	2009	Trivandrum	185000	119	138
Battacharya S	2005	West Bengal	20842	124	262

RISK FACTORS FOR ISCHAEMIC STROKE

Non-Modifiable Risk Factors

Age, ethnicity, gender, race and heredity have been recognized as markers of risk for stroke. Despite these factors being non-modifiable, their presence requires vigorous treatment of risk factors that can be modified.

AGE

Age is the most important risk factor for stroke. For each successive 10 years after the age of 55, the incidence of stroke more than doubles in both sexes.[21]

SEX

Stroke occurrence rates are 1.25 times higher in men. Women being likely to live longer than men, the annual mortality rate among women is higher.[22]

HEREDITARY/ FAMILIAL FACTORS

Probable reasons for genetic tendency for stroke are genetic determinants of other stroke risk factors, and an exposure to environmental or lifestyle risks. Studies suggest that men with a

maternal history of stroke and women with a family history of stroke [23] are at increased risk.

RACE/ ETHNICITY

Stroke incidence and mortality rates differ widely between racial groups. Afro-Americans are at twofold risk of mortality due to stroke as compared to whites.[24] Asians, particularly Chinese and Japanese, have elevated stroke incidence rates.[25]

Potentially Modifiable Risk Factors for Ischemia Stroke

HYPERTENSION

Hypertension is high risk factor for all types of stroke. The relationship of diastolic blood pressure and stroke is log linear throughout normal range of pressure. The systolic blood pressure and stroke had a stronger and consistent relationship than diastolic blood pressure. Hypertensive patients had four times more chances of having stroke, when systolic blood pressure was ≥160 mm Hg and/or the diastolic blood pressure was ≥95 mm Hg.[26]

CARDIAC DISEASE

Various cardiac diseases have been proved to increase risk of stroke. Atrial fibrillation (AF) is one of the most important risk factor. Increasing age predisposes to developing AF. After 55years of age, incidence of AF doubles for every ten years. [27] Cardiac valve

abnormalities, especially mitral stenosis, mitral annular calcification and mitral valve prolapse. Calcification of the mitral valve annulus was associated with a doubled rate stroke rate in follow-up.[28]

Recent studies have shown that valvular strands attached to the mitral and aortic valves as risk factor for stroke. These are usually identified by transesophageal echocardiography (TEE). Left atrial enlargement has also been shown to be a well-known risk factor for stroke. A 1cm increment in size of left atrium increased the age-adjusted risk of stroke by approximately two times.[29] Other causes may include anterior wall myocardial infarction and left ventricular aneurysm.

DIABETES AND GLUCOSE METABOLISM

Individuals with diabetes have been shown to be prone to atherosclerosis and have an increased prevalence of atherogenic risk factors specially obesity, hypertension, and dyslipidemia. Diabetes also has been shown to be an independent risk factor for ischemic stroke with a relative risk of 1.8-3.0.[30]

In the Framingham study, impaired glucose tolerance doubled the risk of ischaemic stroke.[31]

TRANSIENT ISCHEMIC ATTACKS (TIA)

The risk of stroke in patients with TIAs is about 4%. After adjusting for major cardiovascular risk factors that predispose a patient to stroke, a TIA remains an important independent risk factor for both stroke and myocardial infarction.[32] TIAs are associated with atherosclerotic lesions at the origin of the internal carotid artery (ICA) or intra cranial portion of ICA, stem of middle cerebral artery, junction of vertebral and basilar arteries, and occlusion of small vessels. Hemispheric ischemic symptoms have usually been associated with high grade stenotic lesions of the internal carotid artery.[33]

LIPIDS

Whereas hypercholesterolemia is an important variable risk factor for coronary heart disease, the relation of lipid variables with ischeamic cerebrovascular disease remains undefined.[34] However, a number of studies clearly support the relation between total and LDL cholesterol and the protective action of HDL cholesterol on extracranial carotid atherosclerosis.[35-37]

CIGARETTE SMOKING

Cigarette smoking increases the relative risk of ischemic stroke almost two times,[38] with apparent dose-response relation, both pack years and cigarettes per day being influential factors. In both the

Nurses' Health Study[39] and the Framingham Study[40] termination of smoking reduces stroke risk.

ALCOHOL

Moderated alcohol intake upto sixty gram per day may reduce cardiovascular disease and stroke. A J-shaped association was found between moderate alcohol consumption and ischemic stroke.[41] Increased consumption of alcohol has been shown to increase the risk for ischemic stroke.[42] Hypertension, arrhythmias, hyperviscosity, hematocrit changes, clotting factor changes and increased platelet aggregation as a consequence of binge drinking may contribute to the development of stroke.

ILLICIT DRUG USE

Drug abuse accounts for around 10% of young adult stroke. Abuse with cocaine is related to stroke.[43] Other drugs implicated in stroke are heroin, amphetamines, D-Lysergic Acid, and marijuana.

LIFESTYLE FACTORS

Diverse lifestyle factors like obesity, physical activity, diet, and acute triggers such as emotional stress have been linked with increased stroke risk. Obesity has been associated with higher levels of blood pressure, blood glucose, and serum lipids, which are independent risk factors for stroke. There is a protective effect of moderate physical

activity on stroke in both men and women.[44] Increased intake of fish rich in unsaturated fatty acids, green tea, and milk were protective for stroke, while food intake rich in fat and cholesterol have been shown to be harmful.[45]

ORAL CONTRACEPTIVES

In recent times, a study of low-dose oral contraceptives (<50 μg estrogen) revealed no increased risk of stroke in more than 3.6 million woman-years of observation.[46]

MIGRAINE

Though migraine has been recognized as an independent risk factor for ischemic stroke in men older than 40 in the Physicians' Health Study, [47] no association has been demonstrated by other studies.

HEMOSTATIC AND INFLAMMATORY FACTORS

Hemostatic factors have not been associated with increase in incidence of cardiovascular disease. However two studies linked fibrinogen to increased stroke risk. Fibrinogen increases viscosity, atherogenesis, platelet aggregation and enhances clot creation that act as the substrate for thrombin.[48]

The tissue-type plasminogen activator (TPA) system, has also been shown to be independently related with risk of stroke.[49]

HOMOCYSTEINE

Blood levels of homocysteine are determined genetically and altered by intake of vitamins B6, vitamin B12, and folic acid. High homocysteine level is a strong, independent risk factor for stroke in middle-aged men.[50]

GENETIC FACTORS

Recently a single gene disorder responsible for ischemic stroke has been described. The gene for cerebral autosomal dominant arteriopathy with sub cortical infarct and leukoencephalopathy (CADASIL) has been localized to chromosome 19 which also hosts the gene for Familial Hemiplegic Migraine. Other genetic disorders associated with stroke include Ehler Danlos Syndrome, Marfan's Syndrome, Sickle cell disease and Protein C and Protein S Deficiency, Familial Cerebral Amyloid angiopathy, mitochondrial cytopathy, and dysfibrinogenemia.

Table 4: Risk Factors for Stroke[51]

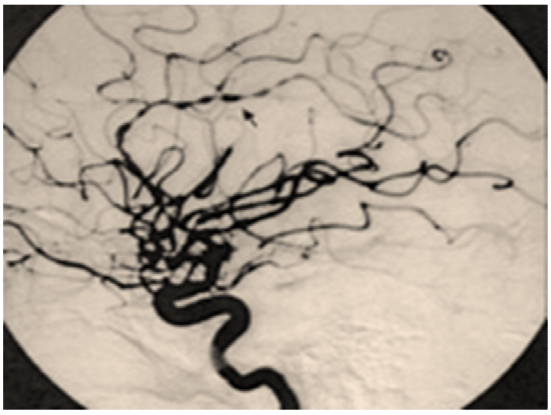
Well-documented risk factors	Less well-documented risk factors
Modifiable, value established	**Potentially modifiable**
Hypertension	Cardiac disease
Cardiac disease	Cardiomyopathy
Atrial fibrillation	Segmental wall motion abnormalities
Infective endocarditis	Nonbacterial endocarditis
Mitral stenosis	Mitral annular calcification
Recent large myocardial infarction	Mitral valve prolapse
Cigarette smoking	Valve strands
Sickle cell disease	Spontaneous echocardiographic contrast
Transient ischemic attacks	Aortic stenosis
Asymptomatic carotid stenosis	Patent foramen ovale
Potentially modifiable	Atrial septal aneurysm
Diabetes mellitus	Elevated blood cholesterol and lipids
Hyperhomocysteinemia	Use of oral contraceptives
Left ventricular hypertrophy	Consumption of alcohol
Non-modifiable	Use of illicit drugs
Age	Physical inactivity
Gender	Obesity
Hereditary/familial factors	Elevated hematocrit
Race/ethnicity	Dietary factors
Geographic location	Hyperinsulinemia and insulin resistance
	Acute triggers (stress)
	Migraine
	Hypercoagulability and inflammation
	Fibrin formation and fibrinolysis
	Fibrinogen
	Anticardiolipin antibodies
	Genetic and acquired causes
	Subclinical diseases
	Intimal-medial thickness
	Aortic atheroma
	Socioeconomic features
	Non-modifiable
	Season and climate

Table 5: Causes for Ischemic Stroke[52]

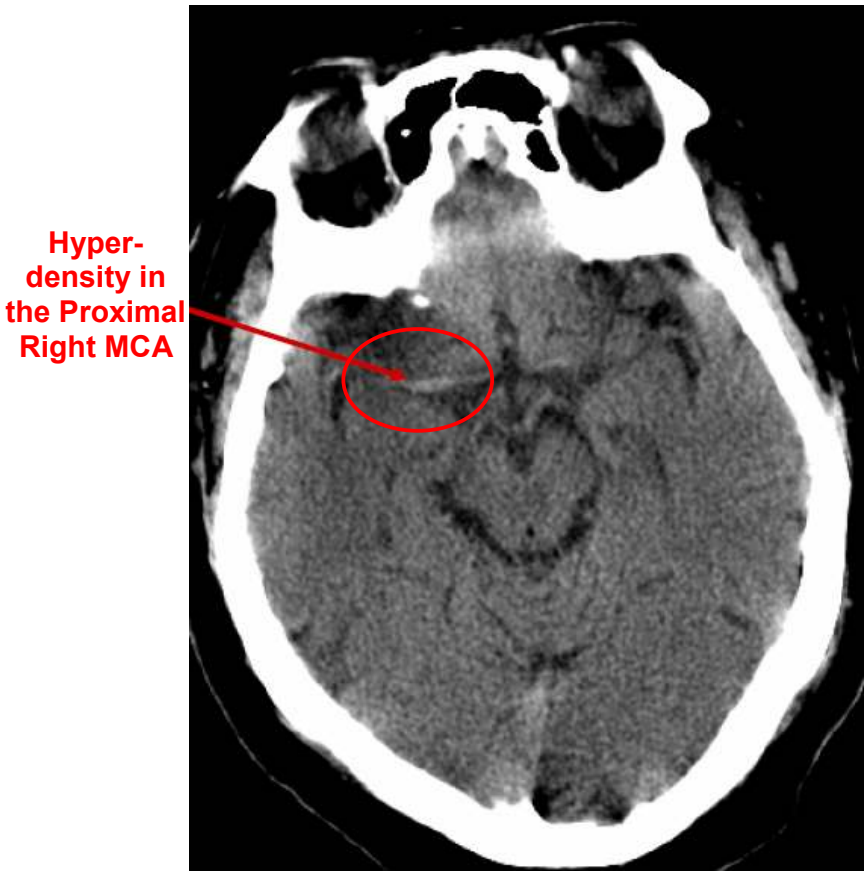
Common Causes	Uncommon Causes
Thrombosis	**Hypercoagulable disorders**
Lacunar stroke (small vessel)	Protein C deficiency
Large vessel thrombosis	Protein S deficiency
Dehydration	Antithrombin III deficiency
Embolic occlusion	Antiphospholipid syndrome
Artery-to-artery	Factor V Leiden mutation
Carotid bifurcation	Prothrombin G20210 mutation
Aortic arch	Systemic malignancy
Arterial dissection	Sickle cell anemia
Cardioembolic	β-Thalassemia
Atrial fibrillation	Polycythemia vera
Mural thrombus	Systemic lupus erythematosus
Myocardial infarction	Homocysteinemia
Dilated cardiomyopathy	Thrombotic thrombocytopenic purpura
Valvular lesions	Disseminated intravascular coagulation
Mitral stenosis	Dysproteinemias
Mechanical valve	Nephrotic syndrome
Bacterial endocarditis	Inflammatory bowel disease
Paradoxical embolus	Oral contraceptives
Atrial septal defect	Venous sinus thrombosis
Patent foramen ovale	Fibromuscular dysplasia
	Vasculitis
	Systemic vasculitis
	Primary CNS vasculitis

Common Causes	Uncommon Causes
Atrial septal aneurysm Spontaneous echo contrast	Meningitis (syphilis, tuberculosis, fungal, bacterial, zoster) **Cardiogenic** Mitral valve calcification Atrial myxoma Intracardiac tumor Marantic endocarditis Libman-Sacks endocarditis Subarachnoid hemorrhage vasospasm **Drugs :** Cocaine, amphetamine Moyamoya disease Eclampsia

Plate : 1 - Cerebral Angiogram



Early Stroke Findings on CT – 1



IMAGING IN STROKE

Radiological Tests:

- Cerebral Angiogram
- Computed Tomography (CT)
  - ✓ With or without contrast
  - ✓ CT angiogram (CTA)
- Magnetic Resonance Imaging (MRI):
  - ✓ With or without contrast
  - ✓ T1 or T2 weighted (T1WI, T2WI)
  - ✓ Fluid attenuated inversion recovery(FLAIR)
  - ✓ Diffusion weighted image (DWI)
  - ✓ MR angiogram

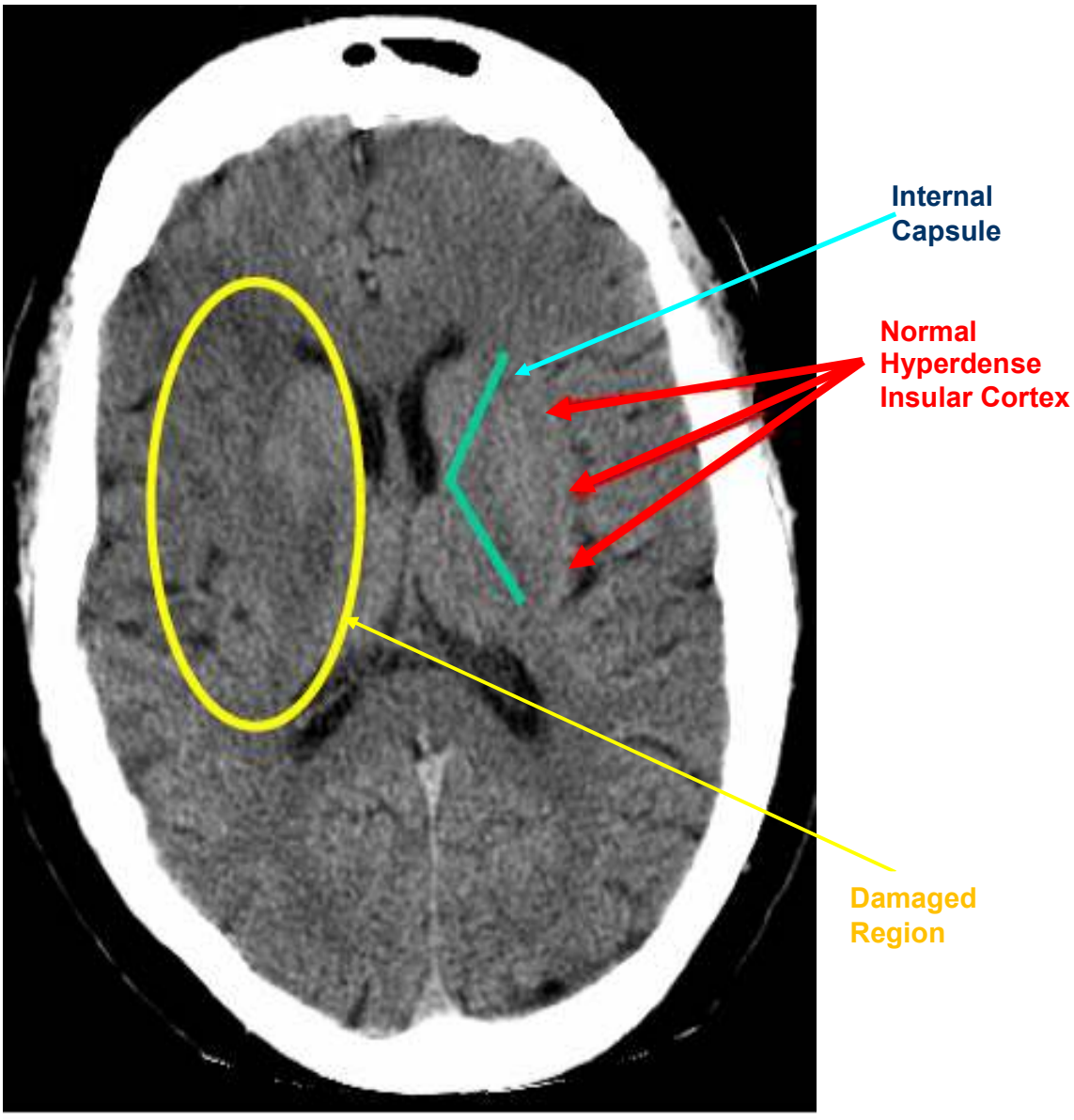
CEREBRAL ANGIOGRAM

- Gold standard in the past
- Outdated and replaced by MRI/MRA
- High risk of producing further thrombus formation in brain and causing renal failure

CT WITHOUT CONTRAST

- Distinguish between ischemic and hemorrhagic stroke.
- Normal CT in patient with <3 hrs of symptoms → can begin tissue plasminogen activator therapy if there is no other contraindications.

Plate 2 : Early Stroke Findings on CT -1



CT FINDINGS IN CEREBRAL INFARCTION [53, 54]

<12 HRS – THE HYPERACUTE PHASE

- Normal 50-60%
- Hyperdense artery (dense MCA sign)
- Obscuration of the lenticular nucleus
- Loss of gray-white interfaces (insular ribbon sign)

12-24 HRS – THE ACUTE PHASE:

- Sulcal effacement
- Low density basal ganglia

24 HOURS – 6 WEEKS – THE SUBACUTE PHASE:

- Increasing mass effect
- Wedge-shaped low density area involving gray and white matter
- Possible hemorrhagic transformation

> 6WEEKS – THE CHRONIC PHASE:

- Parenchymal hypodensity with well-defined margins
- Necrotic areas in larger ischaemic foci evolve towards porencephalic cavitation, with accompanying dilation of the ipsilateral ventricle and adjacent subarachnoid cisterns
- Some cases may show an ipsilateral displacement of midline structures

MRI Findings in Cerebral Infarction [54]

Immediate : Hyperintense on DWI, IV contrast enhancement, Perfusion alterations

<12 hrs : Sulcal effacement, gyral edema, loss of gray-white interfaces on T1

12 to 24 hrs : Hyperintensity on T2, Meningeal enhancement adjacent to infarct, Mass effect

1 to 3 days : IV and meningeal enhancement begin decline, Signal abnormalities striking on T1WI, T2WI, Possible hemorrhagic transformation

MRI-T2 Weighted Image : T2W: good anatomical detail, T2 signal hyperintensity in R, MCA territory: R insula, basal ganglia and internal capsule

MR-DWI : Findings similar to those in T2WI → hyper-intensityin R, T2 signal hyper-intensity in R, MCA territory: R insula, basal ganglia and internal capsule. Fluid attenuated inversion recovery images are particularly useful in hyperacute cortical infarct within 3 hours of onset. [55]

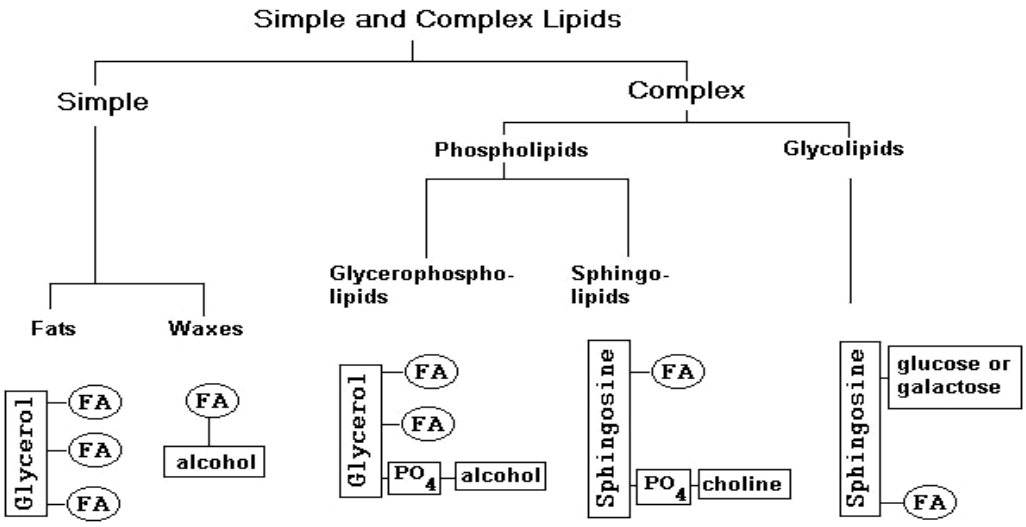
SERUM BIOCHEMISTRY

Serum Lipids

Lipids are water insoluble but are soluble in alcohol and other organic solvents.[56] When dietary fats are digested and absorbed into the small intestine, they progressively re-form into triglycerides, which are then packaged into lipoproteins.

CLASSIFICATION OF LIPIDS

Figure 6: Classification of Lipids



1. Simple Lipids

   Neutral fats – Triglycerides, Waxes

2. Conjugated Lipids (polar lipids)

   Phospholipids, Cerebrosides, Sulfolipids

3. Derived Lipids

Fatty acids, Fatty alcohols, Fatty aldehydes, Hydrocarbons and Vitamins A, D, E, K

4. Miscellaneous

Soaps, Colouring matters, Oxidative polymers, Thermal polymers.

Cholesterol

Cholesterol is a waxy steroid of fat that is produced in the liver or intestines and reduces the fluidity of cell membrabes.[57] It is also an important component for the production of bile acids, steroid hormones, and Vitamin D. Cholesterol circulates in the bloodstream as lipoproteins.

Low-density lipoprotein (LDL) cholesterol is the "bad" cholesterol because elevated LDL levels are related with an increased risk of coronary artery disease.

- ✓ LDL levels less than 100 mg/dL are considered optimal.
- ✓ LDL levels between 100 – 129 mg/dL are considered near or above optimal.
- ✓ LDL levels between 130 – 159 mg/dL are considered borderline high.
- ✓ LDL levels between 160 – 189 mg/dL are considered high.
- ✓ LDL levels at or above 190 mg/dL is considered very high.

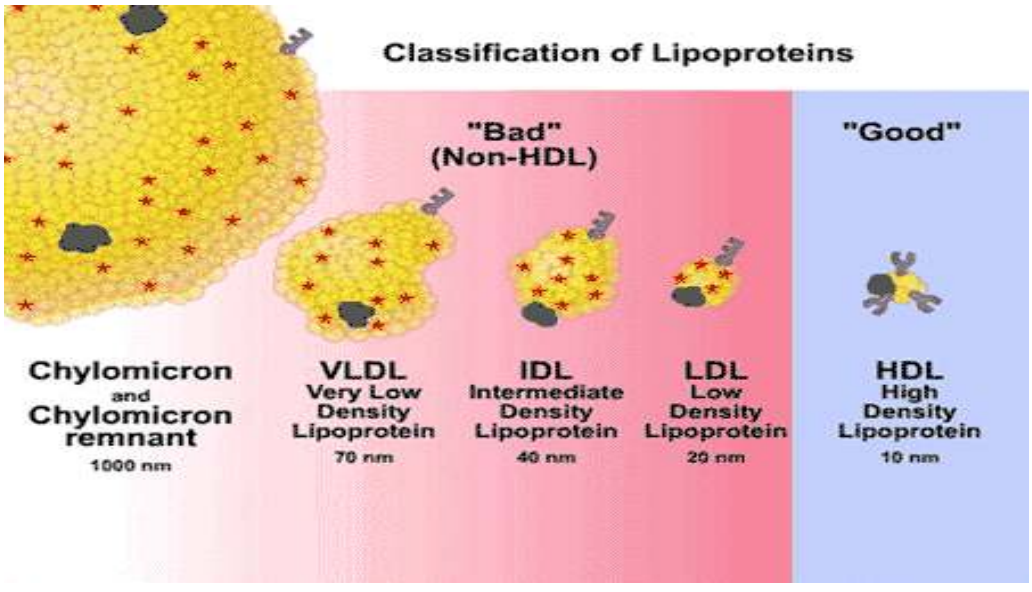
A HDL level more than 60 mg/dL is considered high. A high HDL level is considered very healthy, since it has a protective role against heart disease. An undesirable level of HDL is any level below 40 mg/dL. In this case, low HDL levels may contribute to heart disease.

Lipoprotein

A lipoprotein consists of a nonpolar lipid core and a single surface layer of amphipathic lipids. Lipids usually do not travel alone in the blood. Instead, they bind to a protein that will transfer it to its correct destination in the body.[58]

CLASSIFICATION OF LIPOPROTEINS

Figure 7: Classification of Lipoprotein



The different types of lipoproteins circulating in the body are,

- ✓ Chylomicrons
- ✓ Very low density lipoproteins (VLDL)
- ✓ Intermediate density lipoproteins (IDL)
- ✓ Low density lipoproteins (LDL)
- ✓ High density lipoproteins (HDL)

These particles transport insoluble lipids in the blood can be harmful (VLDL, IDL, LDL) or useful (HDL) to our health.

During the first pass through the gastrointestinal system, lipoproteins are wrapped as chylomicrons, secreted into the circulation, are transformed into chylomicron remnants, and then finally transported to the liver [(59)]. There they are re-packaged as a series of smaller, denser lipoprotein "particles" and are re-secreted back into the circulation. However a working knowledge of the elements of lipid metabolism is required in order to ensure proper recognition and supervision of dyslipoproteinemia.[(60)] Small, dense LDL particles, with the minor particles being more atherogenic.

In the new US National Cholesterol Education Program (NCEP) guidelines, the "non-HDL" sub fraction of cholesterol has become the new objective of measurement and treatment.[(61)] To compute this

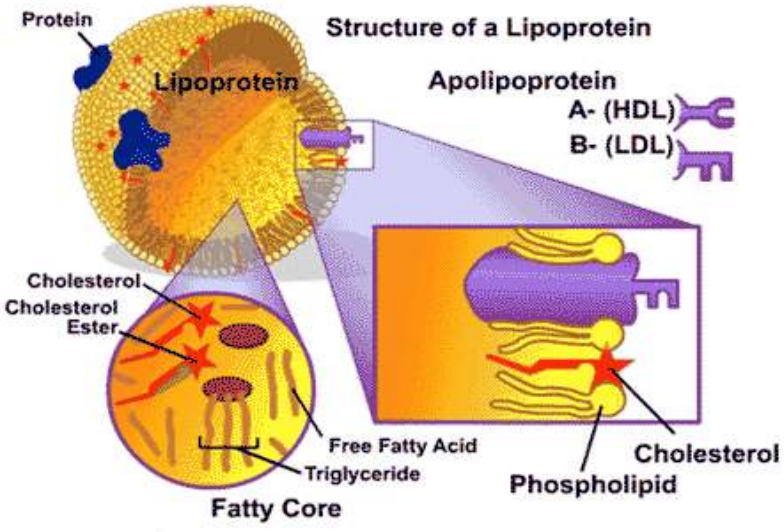
parameter, the clinician measures total cholesterol (TC) and then determine the non-HDL level according to the formula:

$$\text{Non-HDL} = \text{TC} - \text{HDL}$$

STRUCTURE OF LIPOPROTEIN

The lipoprotein molecules that we ingest are repackaged into particles so that they can be combined into a food delivery and fat elimination system.[62]

Figure 8: Structure of Lipoprotein



As shown in the figure, all of these particles are assembled as lipid "globules," or particles, with a monolayer phospholipid membrane.

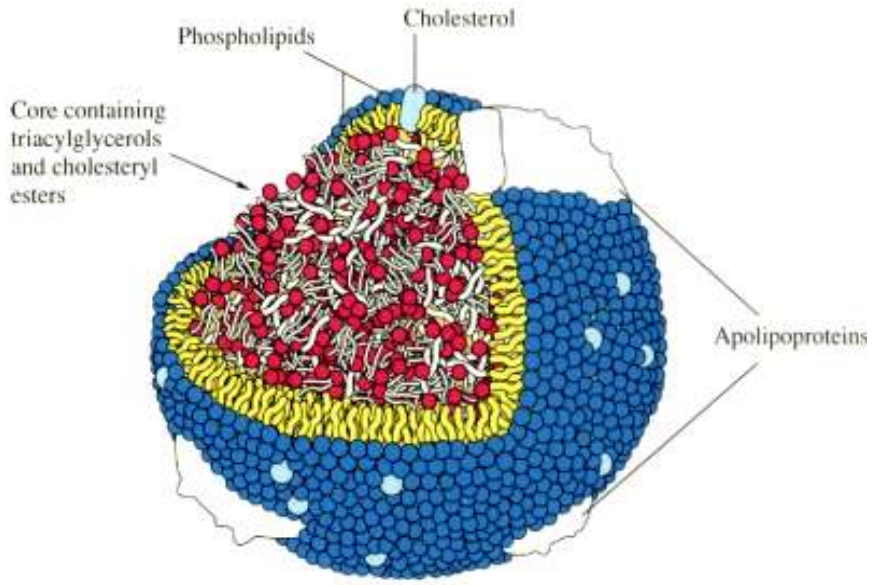
The enlargement of the cell membrane on the figure shows the components of the monolayer phospholipid membrane.The lower left of the figure affords a look "inside" the lipoprotein particle, where we see the "fatty core," consisting of cholesterol, cholesterol esters, triglycerides (the dark brown "jelly fish"), and free fatty acids (the "legs" of the jelly fish).

All lipoprotein particles are built in this manner; the particles vary in their size and density or, in the case of the HDL vs non-HDL, in the apolipoprotein molecule implanted in the surface membrane (Apo A vs Apo B).

Apolipoproteins

Cholesterol and triglycerides are transported everywhere in the body by the lipoproteins: HDL, LDL, IDL, VLDL, and chylomicrons.[63] These lipid-protein complexes all have alike structures but are different sizes, densities and compositions. The outside shell is a monolayer of polar lipids: phospholipids and free cholesterol. The core comprises neutral lipids: triglycerides and cholesterol esters.

Figure 9: Structure of Apolipoprotein



Apolipoproteins relate with transportation proteins and lipoprotein receptors as well as being co-factors for lipolytic enzymes. Lipoproteins are used in blend with other factors such as weight, blood pressure and family history to assess cardiovascular risk and to select and monitor treatment. [64]

CLASSIFICATION OF APOLIPOPROTEINS

Apolipoprotein A-1 and A-11

Apo A-I and Apo A-II are the core protein components of HDL cholesterol. [65] HDL participates in removing excess cholesterol from the tissues for removal by the liver. Apo A-I is non-atherogenic but increased levels of Apo-II appear to promote atherosclerosis by moving Apo A-I in HDL and inhibiting reverse cholesterol transport.

Apolipoprotein B

Apo B is a component of LDL cholesterol and allows tissue cells to take up cholesterol. Elevated levels of Apo B indicate increased cardiovascular threat even when total and LDL cholesterol levels are within the typical range.[66]

Apolipoprotein C-I1 and C-11

Apo C-II and Apo C-III have antagonistic excitatory and inhibitory properties on lipoprotein lipase, which breaks down lipoproteins and hydrolyses triglycerides in VLDL and chylomicrons for absorption into tissue cells. Apo C-II deficiency leads to hypertriglyceridemia; genetic Apo C-III deficit increases the rate of triglyceride clearance. Low Apo C-II and raised Apo C-III levels are associated with a variety of diseases such as type 2 diabetes, hypertriglyceridemia and hyperbilirubinemia.

Apolipoprotein E

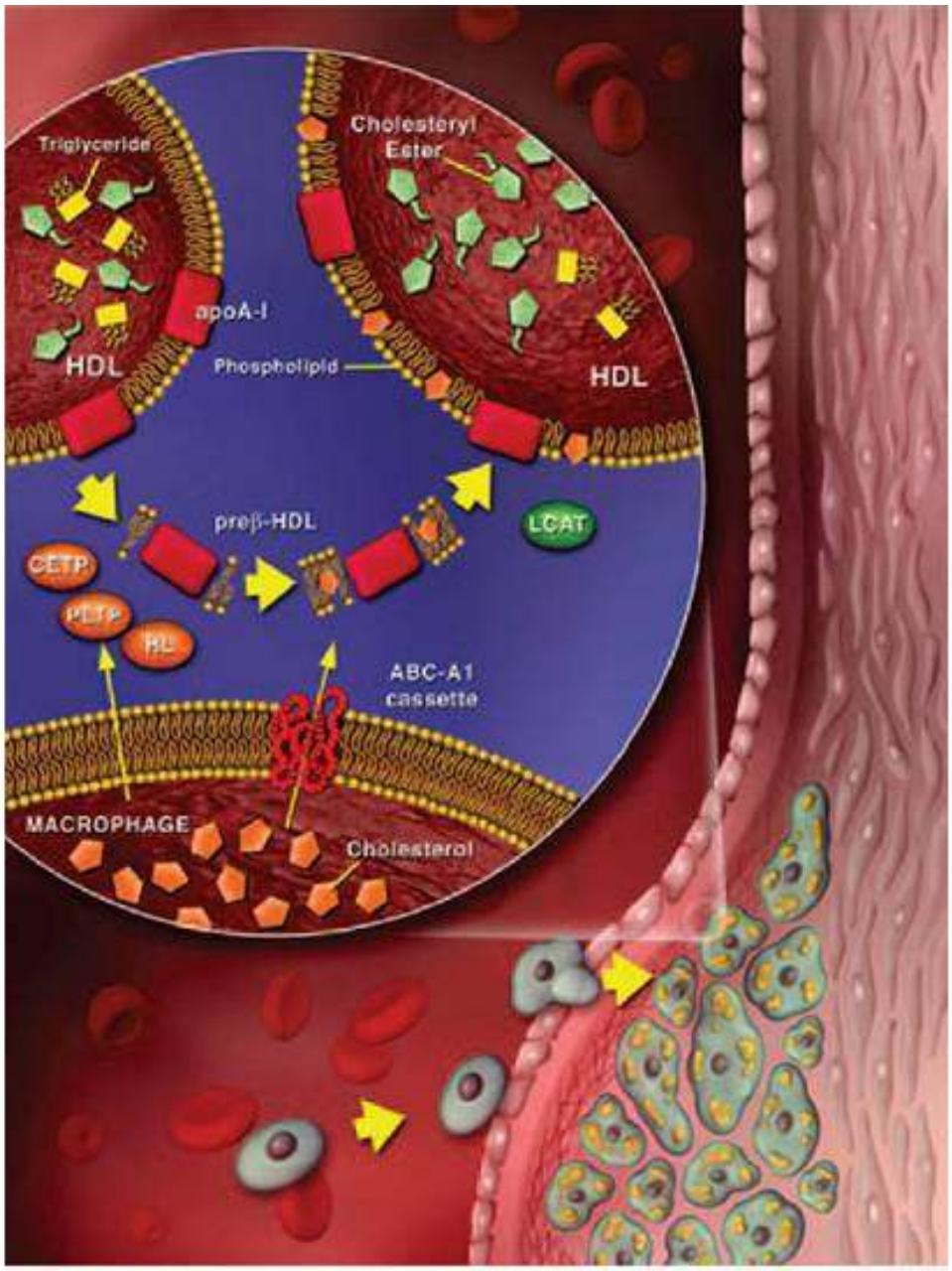
There are three comparable isoforms of Apo E: Apo E2, E3 and E4 with E3 being the most common. Apo E has a variety of purposes depending on which lipoprotein it is in. Apo E deficiency gives rise to high cholesterol and triglyceride levels, promoting atherosclerosis. The polymorphism has been related with diseases other than

cardiovascular disease, for example E4 is implicated in Alzheimer's disease.[67]

Lipoprotein Metabolism

Lipoprotein metabolism has a crucial role in atherogenesis. It includes the transport of lipids, particularly cholesterol and triglycerides, in the blood.[68] The intestine absorbs dietary fat and packages it into chylomicrons, which are transported to peripheral tissues. The enzyme lipoprotein lipase breaks down chylomicrons in muscle and adipose tissues, and fatty acids are taken up by these tissues.[69] The enzyme lipoprotein lipase is localized to the walls of blood capillaries. Chylomicron remnants are taken in the liver by receptor mediated endocytosis apo E. Very-low-density lipoproteins (VLDLs) are synthesised in the liver and intestine. They contain endogenous triglycerides and are hydrolysed by lipoprotein lipase to intermediate-density lipoproteins (IDLs). IDLs are then taken up by the liver through binding to the LDL receptor (LDLR), as well as other routes or are converted to LDL. LDL makes cholesterol available to extra hepatic tissues. Liver and other extra hepatic tissues express LDL (Apo B-100, E) receptor. Approximately 70% of LDL is degraded in the liver with the remainder portion in the extra hepatic tissues.

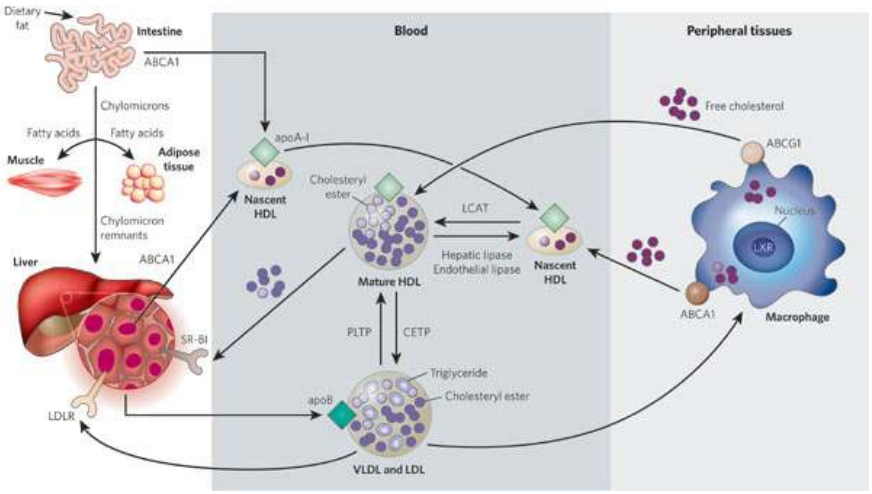
Plate 3 : CETP and its role in HDL metabolism



The figure depicts how the protein CETP, phospholipid Transfer protein (PLTP) and hepatic lipase (HL) acts upon HDL to generate new HDL particles that results in a reduction in cholesterol in atherosclerotic lesions

High-density lipoproteins (HDLs) are formed in the intestine and the liver through the secretion of lipid-free ApoA-I. HDL acts as a repository for the apoC and apoE required in the metabolism of chylomicrons and VLDL.

Figure 10: Lipoprotein metabolism

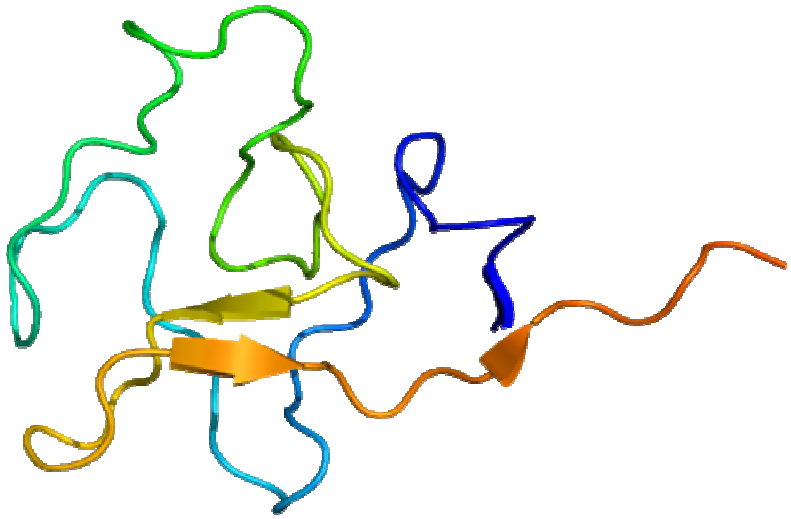


HDLs facilitate the efflux of cholesterol from tissues through the actions of ABCA1(reverse cholesterol transport). Nascent HDL consists of discoid phospholipid bilayer containing apoA and free cholesterol. The cholesterol in nascent HDLs is esterified to cholesteryl ester by lecithin cholesterol acyl transferase (LCAT).

The cholesterol in HDLs circulates back to the liver through uptake by the receptor SR-BI, and by transfer to LDLs and VLDLs through the cholesteryl ester transfer protein (CETP). The lipid content of HDLs is altered by the enzymes hepatic lipase, endothelial lipase and by the transfer proteins, affecting HDL catabolism.[70]

LIPOPROTEIN (A) – LP (A)

Figure 12: Structure of Lipoprotein (a)



Lipoprotein(a) is a lipoprotein subclass. It is an accepted risk factor for atherosclerotic diseases such as coronary heart disease and stroke. [71]

Lp(a) has prebeta pattern in Electrophoresis, size being 4.9A°, and mass 3.8-4.60 x 10^{-6}. The half-life of Lp(a) in the circulation is about three to four days.

Lipoprotein(a) consists of an LDL-like particle and the particular apolipoprotein(a), which is covalently bound to the apoB-100 of the LDL like element. Lp(a) plasma concentrations are extremely heritable and mainly controlled by the apolipoprotein(a) gene situated on chromosome 6q26-27. Apo(a) proteins differ in size due to articulation at the protein level.[72]

There is an inverse correlation between the size of the apo(a) gene kringle IV repeats resulting in size polymorphism and the Lp(a) plasma concentration. This is caused by a variable rate of degradation of the apo(a) protein prior to its secretion for Lp(a) assembly.[73] Apo(a) is articulated by liver cells, and the assembly of apo(a) and LDL particles appears to take place at the outer hepatocyte surface. Lp(a) levels may be influenced in many conditions like Nephrotic syndrome, malignancies, chronic renal failure, and hypothyroidism. [74-80]

Lipid variables and the risk of stroke

TOTAL CHOLESTEROL (TC) AND STROKE

Initial studies found no consistent results of elevated serum TC values as a predictor of stroke related mortality, with few studies inversely correlating TC values with death due to stroke. A meta-analysis of 13000 strokes in a total of 450000 people, found no significant association between serum TC levels and stroke. [81] The Framingham heart study found a variable yet positive correlation between TC levels and the risk of cerebrovascular disease among women of different age groups. Studies have showed an inverse association between TC values and the risk of intracerebral

haemorrhage, independent of age and sex. However, a significant linear relation was also found between TC values and ischaemic stroke.[81]

Large studies like the Honolulu heart study in migrants from Japan and the Multiple Risk Factor Intervention Trial screening study have shown an upsurge in non haemorrhagic stroke that was seen at the zenith of TC concentrations.

TG CONCENTRATIONS AND STROKE

The postprandial hypertriglyceridaemia is related with carotid artery atherosclerosis.[81] Despite a disagreement between the relationship of serum triglyceride values and the risk of cerebrovascular disease, a log linear association between serum triglyceride concentrations and ishaemic stroke was found. Further, this association was not related to age and sex.[81]

HDL CHOLESTEROL AND STROKE

Many studies have reported an inverse relation between HDL levels and the risk of stroke. [81, 82]

APOLIPOPROTEIN E (APO E) PHENOTYPES AND STROKE

Apo E phenotypes have been variably associated with stroke. While apo E2 and apo E4 have been found to increase the risk, apo

E3/E3 phenotype has been associated with a protective effect against ischemic stroke.[83]

LP (A) AND STROKE

Apart from the well-established risk factors for strokes (such as increasing age, hypertension, diabetes, smoking, or the presence of vascular disease), the possibility that Lp(a) is a risk factor for ischaemic stroke has been shown in several studies.[81]

Studies favouring Lp(a) as a risk factor for stroke

In a case control study, serum Lp(a) values were expressively greater in patients with ischaemic stroke in comparison to healthy individuals. This difference was also obvious in a subgroup of subjects between 30 to 69 years.[81]

A Meta-analysis by Smoulder et al demonstrated that Lp (a) is a risk factor for incident stroke.[82] Bostom et al found Lp (a) to be an independent indicator for stroke.[83] Nagayama et al showed that liprotein (a) level is very significant in atherothrombotic stroke ($p<0.01$)[84].

Vavernova et al studied Lp(a) values in 45 patients with stroke (younger than 55 years of age) and their first degree relations. [85] They reported increased serum Lp (a) levels in patients with stroke. They also reported that Lp (a) levels were genetically determined.

Van Kooten and colleagues found an increased Lp(a) to be associated with increased risk of stroke while not influencing the stroke characteristic or the prognosis in such patients.[86]

Peng et al examined the relation between serum lipids, apoE genotypes, and the risk of ischaemic stroke in a case controlled study of 90 patients. They found that serum Lp(a) concentrations and the apoE4 genotype were prominent predictors for ischaemic stroke in addition to the previously established risk factors such as hypertension, personal history of stroke, and smoking.[87]

Kario and colleagues reported that a hypercoagulable state, endothelial damage, and increased Lp(a) concentrations predisposed asymptomatic, high risk, elderly Japanese patients (aged 44 to 93 years) to silent multiple lacunar strokes. Raised Lp(a) values specially those > 30 mg/litre was found to be associated with more number of lacunes.[88]

Studies not supporting Lp (a) as a risk factor for stroke

The association between Lp(a) and stroke has been disputed by some investigators. Hachinski et al,[89] in a case control study, demonstrated that increased LDL and TG levels correlated with atherothrombotic stroke risk, while there was no significant variance

in the Lp(a) concentrations or the distribution of apoE phenotypes among patients and controls.

In a study conducted in Department of Bio-chemistry Sri Devaraj Medical College, Kolar showed no statistical significant difference in Lp(a) between controls and thrombotic stroke [90].

The possibility of anticipating ischaemic stroke by the estimation of plasma Lp(a) concentrations and antibodies to Chlamydia pneumoniae was investigated by Glader et al.[91] They found no relationship between baseline plasma Lp(a) values, the presence of anti - C. pneumoniae antibodies, and future ischaemic cerebral infarctions. They found no interaction between high Lp(a) values and anti-C. pneumoniae antibody titres.

A prospective study in Finland found no relationship between Lp(a) or plasma homocysteine and atherosclerosis.[92]

Interventions for the reduction of Lp (a)

DIETARY MODIFICATION

Saturated fatty acids, n-3 polyunsaturated fatty acids, palm oil may slightly reduce Lp(a) values. [93]

NICOTINIC ACID

Nicotinic acid has a good but inconsistent, effect on Lp(a) concentrations. Large doses of this drug are difficult to tolerate. [94]

STATINS

The Scandinavian simvastatin survival study (4S) showed that simvastatin at 20-40 mg daily reduced the combined occurrence of TIA and stroke by 29% [36]. The cholesterol and recurrent events (CARE) trial evaluated the role of pravastatin (40 mg daily) in reducing the relative risk of stroke. It was shown that it reduced the risk by as much as 32%, over a median follow up period of five years. In the long term interference with pravastatin in ischaemic disease (LIPID) study, pravastatin (40 mg daily) reduced the relative risk of stroke by 19%. These beneficial effects on stroke and myocardial infarction occur despite a statins causing a slight increase in circulating Lp(a) values.

FIBRATES

Fibrates decrease fibrinogen and possibly Lp(a) and oxidised LDL values [95]. In bezafibrate infarction prevention study, gemfibrozil (1200 mg daily) reduced total stroke in comparison to the placebo group. TIA in the same trial was reduced from 4.2% to 1.7%, and carotid endarterectomy was significantly reduced. However, LDL values were fundamentally unchanged.

DIABETES

Tight glycaemic control may beneficially influence Lp(a) values. In type 2 diabetes, glycosylation of Lp(a) has been shown to interfere with its catabolism. [96]

HORMONAL TREATMENT

Hormonal replacement therapy (HRT) associated with a reduction in the risk of evolving coronary artery disease, affects cholesterol, Lp(a), and homocysteine concentrations, especially in postmenopausal women. [97]

Thyroid hormone replacement treatment decreases Lp(a) concentrations, possibly due to its effect upon apo(a) production, or probably Lp(a) assembly.

FUTURE TARGETED INTERVENTION

Lp(a) undergoes further modifications like oxidation and proteolysis after entry into the wall of the artery. These post-translational events could be potential targets for therapeutic intervention in future. [98]

METHODOLOGY

The study was conducted in the Government Mohan Kumaramangalam Medical College, Salem, Tamil Nadu, India. Approval of the Institutional Ethical Committee was obtained prior to the study. In this study the sample size was 80 subjects admitted in the ward during the period of October 2009 to November 2011, who were divided into two groups, 40 cases diagnosed as ischaemic stroke (confirmed by CT brain) and 40 control which was matched for age and gender. The study consists of history taking, clinical examination and biochemical assay. Study subjects were selected after having obtained consent.

All 40 cases were examined and lab investigations were done including CT scan, lipid profile and lipoprotein (a)estimation. All ischaemic stroke patients underwent cardiac evaluation.

Inclusion Criteria for Cases

Patients admitted in the ward with cerebrovascular event and CT scan showing acute large vessel infarct.

Exclusion Criteria for Cases

- ✓ Patients with hemorrhagic stroke.
- ✓ Patient with cardiovascular cause for emboli.

- ✓ Patient on medications altering lipid metabolism (sex steroids, statins)
- ✓ Patients having lacunar infarct.

Inclusion Criteria for Controls

The patients admitted in the ward without any history, clinical findings or CT evidence of any previous cerebral infarct (if available) or cardiac illness like scorpion sting, unknown bite with no signs of envenomation, oleander seed poisoning with no signs of toxicity, acid peptic disease.

Study Parameters

HYPERTENSION

Patients were diagnosed with hypertension if systolic blood pressure ≥ 140 mm of Hg or diastolic blood pressure ≥ 90 mm of Hg or both as per the guidelines of JNC VII report or if the patient was a known hypertensive.

DIABETES MELLITUS

Patients with fasting blood sugar ≥ 126 mg%, 2 hours post prandial blood sugar ≥ 200 mg% and known diabetics on treatment.

SMOKING

A person with history of smoking any tobacco product, regularly or occasionally.

Test Procedures

BLOOD COLLECTION

Blood was collected from all patients using perfectly dry and sterile syringes by Venipuncture done in the cubital fossa.

LIPID PROFILE ESTIMATION

Total cholesterol, LDL, HDL and Triglyceride were estimated by enzymatic method. LDL cholesterol is calculated by using a standard WHO approved formula based on total cholesterol, HDL cholesterol and triglyceride values.

$$\text{LDL cholesterol} = \text{Total cholesterol} - \text{HDL cholesterol} - \frac{\text{triglyceride}}{5}$$

VLDL cholesterol is calculated by using a standard WHO approved formula based on triglyceride values.

$$\text{VLDL} = \frac{\text{triglyceride}}{5}$$

LIPOPROTEIN(A) ESTIMATION

Lipoprotein(a) was estimated by spectrophotometry by measurement of the reflection or transmission properties of a material as a function of wavelength.

Blood Hemoglobin, Sugar, Urea and Serum Creatinine were estimated using auto analyzer.

RESULTS

Lipid parameters and lipoprotein(a) segment in cases were correlated with those of values for controls.

Statistical Methods

The significance of proportions of elevated lipoprotein (a) between cases and controls were found using Fisher exact test and Chi-square test Significance of lipid parameters, lab parameters and lipoprotein (a) between cases and controls were found using student t test.The strength of relationship is found using odds ratio. The effect size is calculated to find the relation of ishaemic stroke on lipoprotein (a). The Pearson Correlation Co-efficient is used to find the exact association between lipid profile and lipoprotein (a).

CHI-SQUARE TEST

Using chi-square test, the distribution of one or more sets of data, is tested whether there is a substantial difference between observed frequencies and expected frequencies.

The chi-square distribution calculation formula is:

$$\chi^2 = \sum_{i=1}^{r} \sum_{j=1}^{c} \frac{(A_{ij} - E_{ij})^2}{E_{ij}}$$

Aij = actual frequency in the i'th row & j'th column

Eij = expected frequency in the i'th row & j'th column

r = number of rows

c = number of columns

The chi-square test can then be used to conclude whether the value of this function is likely to have occurred by chance only, in independent sets of data.

FISHER EXACT TEST

Fisher's exact test is used to determine if there are nonrandom relations between two categorical variables. It is used to calculate the exact P value.

Table 6: Fisher Exact Test

	Category 1	Category 2	Total
Sample 1	**a**	**b**	**a+b**
Sample 2	**c**	**d**	**c+d**
Total	**a +c**	**a +d**	**n**

$$\sum p = \frac{(a+b)!(c+d)!(a+c)!(b+d)!}{n!}\frac{1}{\sum a!b!c!d!}$$

STUDENT T- TEST (INDEPENDENT)

Student T-Test is used to evaluate the differences in means between two groups.

$$t = \frac{\bar{X}_1 - \bar{X}_2}{S_{X_1X_2} \cdot \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}}$$ where $$S_{X_1X_2} = \sqrt{\frac{(n_1 - 1)S_{X_1}^2 + (n_2 - 1)S_{X_2}^2}{n_1 + n_2 - 2}}.$$

PEARSON CORRELATION CO-EFFICIENT AND ITS SIGNIFICANCE TEST

Pearson Correlation is a used to investigate the relationship between two quantitative, continuous variables. Pearson's correlation coefficient (r) is a quantity of the strength of the association between the two variables.

$$r = \frac{\sum (x - \bar{x})(y - \bar{y})}{\sqrt{\sum (x - x)^2 (y - y)^2}}$$

Significance

The t-test is used to prove if the correlation coefficient is significantly different from zero, and, hence that there is proof of a relationship between the two variables. There is then the fundamental assumption that the data is from a normal distribution sampled randomly. If this is not true, the verdicts may well be nullified.

Statistical Software and Tools

Charts, Graphs and Tables were generated using Microsoft Excel and Microsoft Word.

For writing Formulas and equations, Microsoft Math Input panel application was utilized.

The data was analysed using statistical software packages, namely SPSS 17.0 and STATA Calc.

STUDY DESIGN

A case control study consisting 40 ischaemic cerebrovascular disease patients (Cases) and 40 normal individuals (controls) was undertaken to investigate the effect of lipoprotein (a), lipid profile, factors like diabetes, hypertension and smoking on stroke and association of lipoprotein (a) with lipid parameters.

AGE DISTRIBUTION

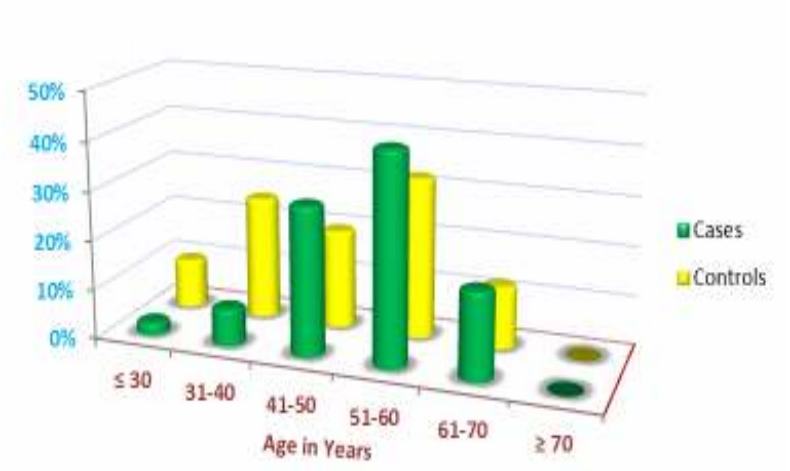
The distribution of the cases and controls falling into different age groups are shown:

Table 7: Age Distribution

Age in years	Cases		Controls	
	No.	**%**	**No.**	**%**
≤ 30	1	2.5	4	10.0
31-40	3	7.5	10	25.0
41-50	12	30.0	8	20.0
51-60	17	42.5	13	32.5
61-70	7	17.5	5	12.5
≥ 70	0	0.0	0	0
Total	40	100.0	40	100.0
Mean ± SD	52.25 ± 9.39		48.30 ± 12.06	
Inference	Samples are age matched with p = 0.106			

SD- standard deviation

Fig 12: Age Distribution



The mean age in our series was 52.25 years with SD 9.39 in the ischaemic stroke (cases) and 48.30 years with SD 12.06 in the controls. Since p>0.05 samples are matched for age.

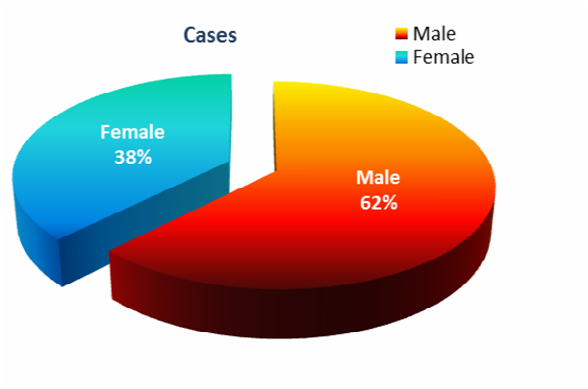
GENDER DISTRIBUTION

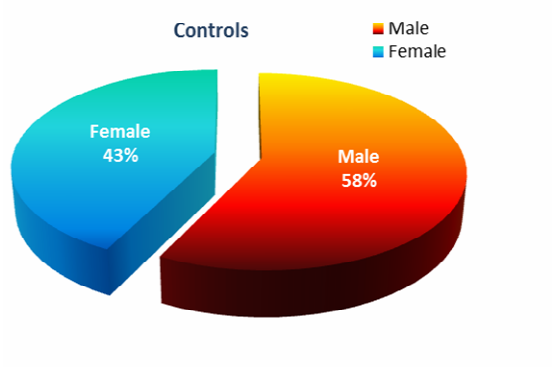
The magnitudes of the cases and controls falling into different gender groups are estimated in this section.

Table 8: Gender Distribution

Gender	Cases		Controls	
	No.	**%**	**No.**	**%**
Male	25	62.5	23	57.5
Female	15	37.5	17	42.5
Total	40	100.0	40	100.0
			p =	1.000
Inference : Samples are matched for gender (p> 0.05)				

Fig 13: Gender Distribution of study population





In our case series, 25 (62.5%) were males and 15 (37.5%) were females. Among the controls 23 (57.5%) were males and 17 (42.5%) were females. The samples are matched for gender.

RISK FACTORS DM, HYPERTENSION & SMOKING

The prevalence of risk factors (Diabetes Mellitus, Hypertension and Smoking) among the Cases and Controls.

Table 9: Risk factors - DM, HTN & Smoking

Risk Factors	Cases		Controls		p Value
	No.	%	No.	%	
DM	19	47.5	12	30.0	0.108
Hypertension	17	42.5	11	27.5	0.160
Smoking	21	52.5	16	40.0	0.262
Inference	The risk factors were increased in cases when compared to controls.				

The prevalence of risk factors (Diabetes Mellitus, Hypertension and Smoking) was higher in the cases in comparison to the controls, but was not statistically significant.

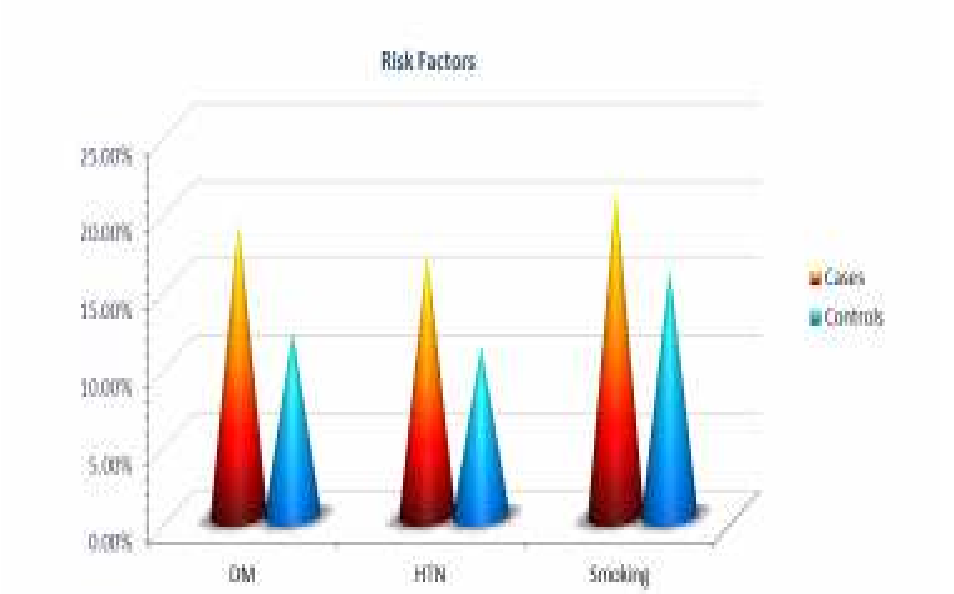


Fig 14: Prevalence of Risk Factors in Study Population

LAB PARAMETERS

The Lab Parameters (Hemoglobin, Urea and Serum Creatinine) are measured and evaluated for the affected individuals (Cases) against the normal individuals (Controls).

Table 10: Lab parameters

Lab Parameters (Mean ± SD)	Cases			Controls			p Value
	Mean	±	SD	Mean	±	SD	
Hemoglobin	11.56	±	2.57	11.18	±	2.06	0.467
Urea	39.40	±	13.62	38.74	±	15.92	0.844
Serum Creatinine	1.16	±	0.38	1.03	±	0.32	0.105

There was no significant difference in the levels of Hemoglobin, Urea and Serum Creatinine between cases and controls.

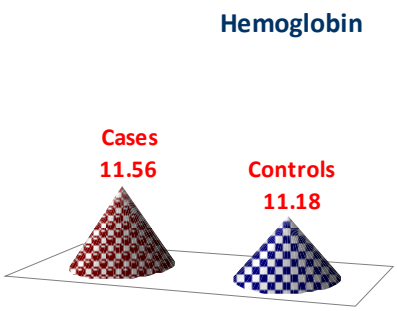


Fig 15: Distribution of Hemoglobin

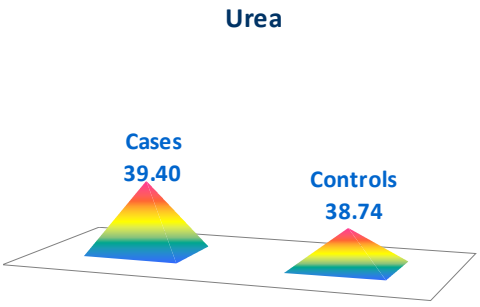


Fig 16: Distribution of Serum Urea

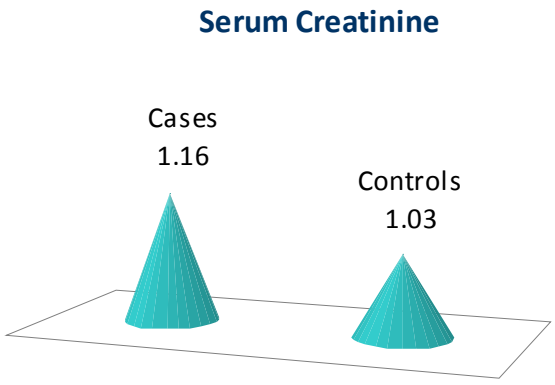


Fig 17: Distribution of Serum Creatinine

LIPID PARAMETERS

The Lipid Parameters (Total Cholesterol, LDL Cholesterol, HDL Cholesterol, and Triglycerides) are measured and evaluated for the affected individuals (Cases) against the normal individuals(Controls).

Table 11: Lipid parameters in cases and controls

Lipid Parameters (Mean ± SD)	Cases			Controls			p Value
	Mean		SD	Mean		SD	
Total Cholesterol	178.00	±	17.27	179.68	±	30.75	0.765
LDL Cholesterol	109.33	±	21.84	108.73	±	32.17	0.923
HDL Cholesterol	37.30	±	6.72	39.23	±	4.12	0.127
Triglycerides	156.93	±	51.28	158.63	±	52.71	0.884

Total cholesterol, LDL Cholesterol, HDL Cholesterol, and Triglycerides between cases and controls are not significant as the p Value > 0.05 in all Lipid parameters. Total Cholesterol, HDL

Cholesterol, and Triglycerides are slightly reduced in cases but, LDL Cholesterol are slightly elevated in cases compared to controls but it was not statistically significant ($p>0.05$).

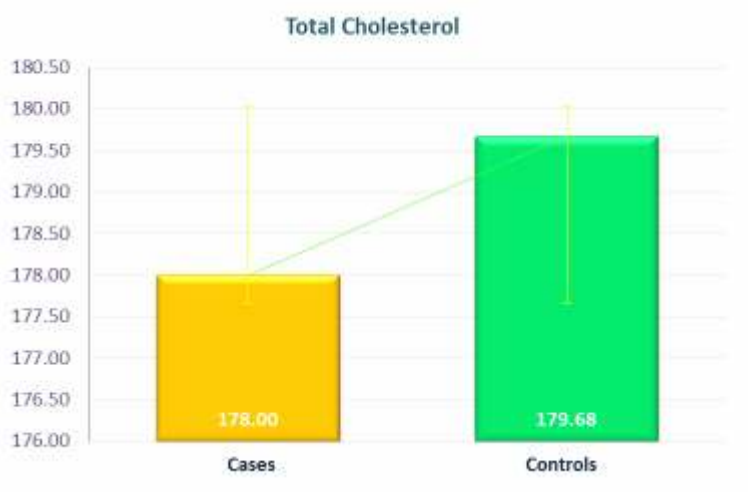


Fig 18: Total cholesterol in study population

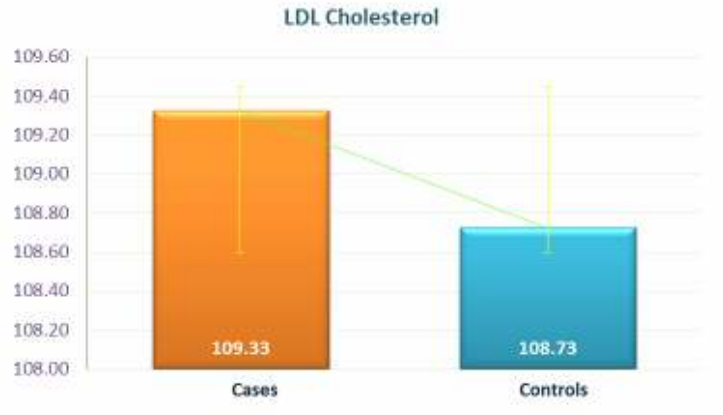


Fig 19: Total LDL in study population

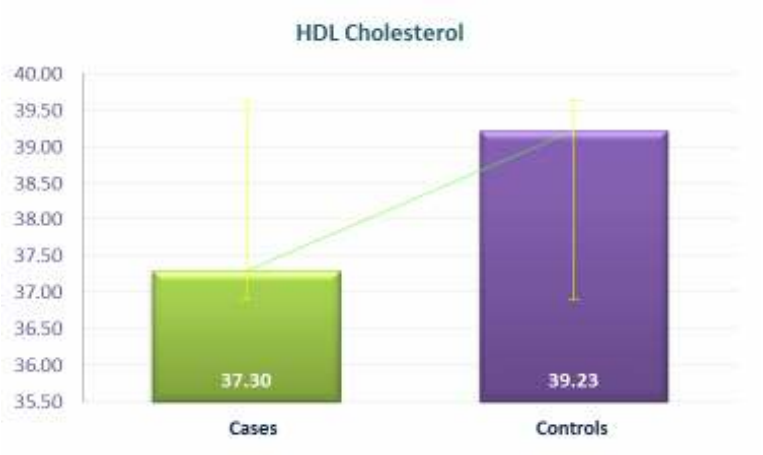


Fig 20: HDL in study population

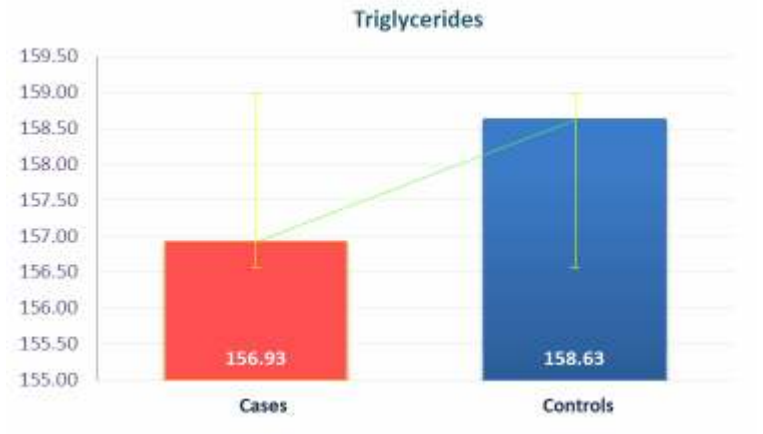


Fig 21: Total triglyceride in study population

LIPOPROTEIN (A) IN CASES AND CONTROLS

The significance of lipoprotein among the cases and controls is studied using the pooled standard deviation and the Effect Size in this section.

Table 12: Lipoprotein (a) in cases and controls

Lipoprotein (a)	Cases			Controls		
Range	8.90	**to**	66.00	5.60	**to**	48.90
Mean | Median	33.46	|	34.00	25.49	|	24.40
Standard Deviation (SD)	15.05			10.17		
Sample Size (*n*)	40			40		
Pooled Standard Deviation	12.842					
Uncorrected Effect Size (*g*)	0.6208					
Corrected Effect Size (*d*)	0.6148					
Inference	Lipoprotein (a) is significantly increased in cases					
	when compared to controls with p =					0.007

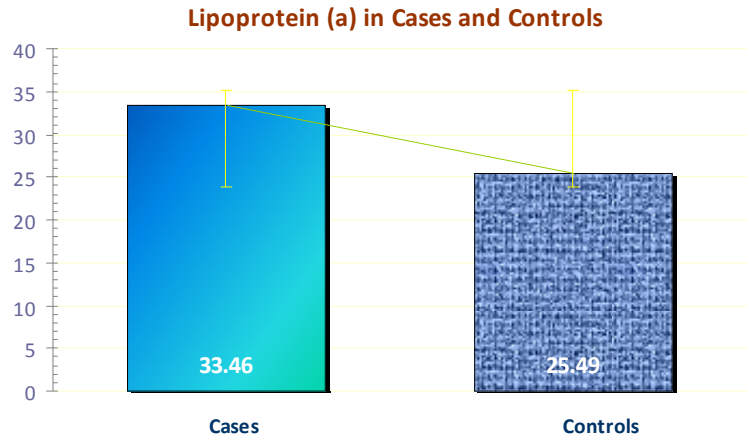


Fig 22: Lipoprotein (a) in study population

While comparing ischaemic stroke patients and controls for lipoprotein (a), the serum lipoprotein (a) levels in ischaemic stroke patients was found 33.46 ± 15.05 mg/dL (mean ± SD), which were significantly (p= 0.007) higher than controls (25.49 ± 10.17 mg/ dL).

ASSOCIATION OF LIPOPROTEIN (A) WITH STROKE

The association of lipoprotein with the stroke is studied in this section for normal (0-30) and elevated levels (>30) with Cases and Controls.

Table 13: Association of Lipoprotein (a) with Stroke

Lipoprotein (a) In mg/dL	Cases		Controls	
	No	%	No	%
Elevated (> 30)	23	57.50	13	32.50
Normal (0 - 30)	17	42.50	27	67.50
Total	40	100	40	100
Inference	Patients with Lipoprotein (a) levels >30mg/dL are 2.81 times more likely to have a Stroke with p = 0.025			

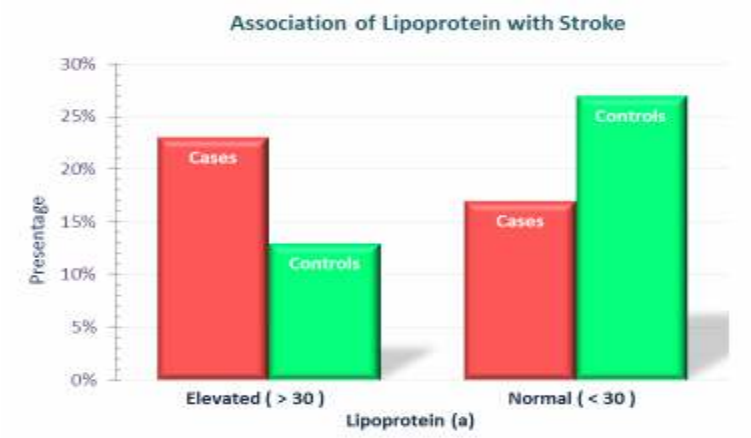


Fig 23: Association of Lipoprotein (a) with stroke

Patients with Lipoprotein (a) levels >30mg/dL are 2.81 times more likely to have a Stroke than normal individuals.

Pearson Correlation of Lipoprotein (a) with Lipid and Parameters

The Pearson Correlation of Lipoprotein with total cholesterol, LDL Cholesterol, HDL Cholesterol and Triglycerides are measured and evaluated for the affected individuals (Cases) against the normal individuals (Controls).

Classification of Correlation Co-efficient (r)

Up to 0.1	Trivial correlation
0.1-0.3	Small correlation
0.3-0.5	Moderate correlation
0.5-0.7	Large correlation
0.7-0.9	Very large correlation

Table 14: Pearson Correlation of Lipoprotein (a) with Lipid Parameters

Pearson Correlation of Lipoprotein (a) with Lipid Parameters		
Lipid Parameters	**Cases**	**Controls**
Total Cholesterol	-0.078	0.060
LDL Cholesterol	0.006	-0.108
HDL Cholesterol	-0.095	-0.044
Triglycerides	-0.080	0.521

The study proves that there inconsequential significance or only a small significance in few lipid parameters. Triglyceride levels are largely correlated in controls.

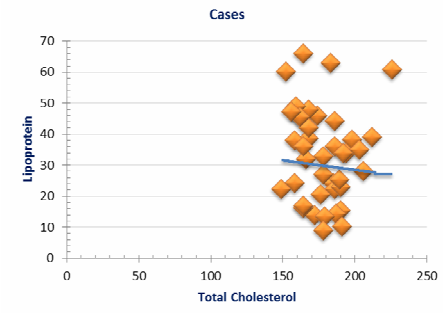


Fig 24: Correlation of Lp (a) with cholesterol in cases

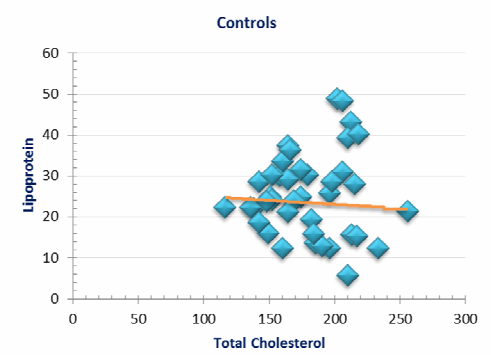


Fig 25: Correlation of Lp (a) with cholesterol in controls

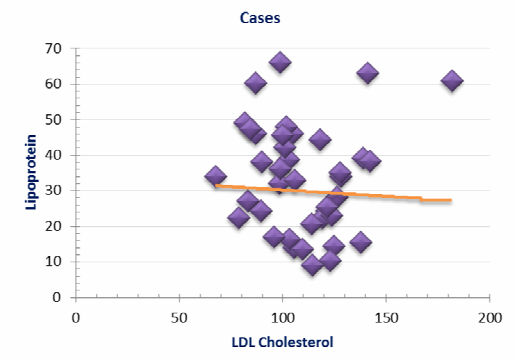


Fig 26: Correlation of Lp (a) with LDL in cases

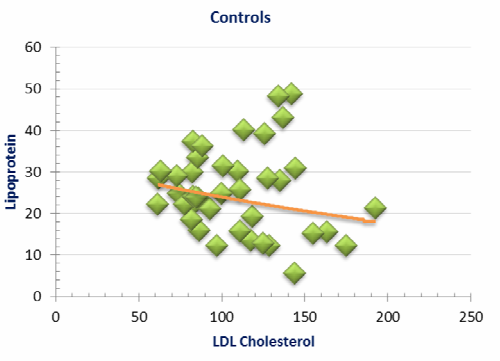


Fig 27: Correlation of Lp (a) with LDL in controls

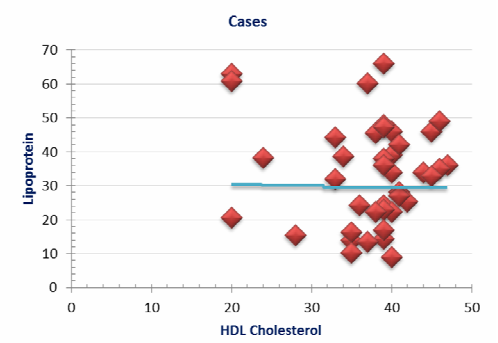


Fig 28: Correlation of Lp (a) with HDL in Cases

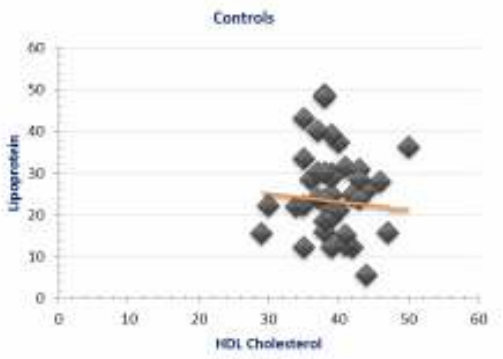


Fig 29: Correlation of Lp (a) with HDL in Controls

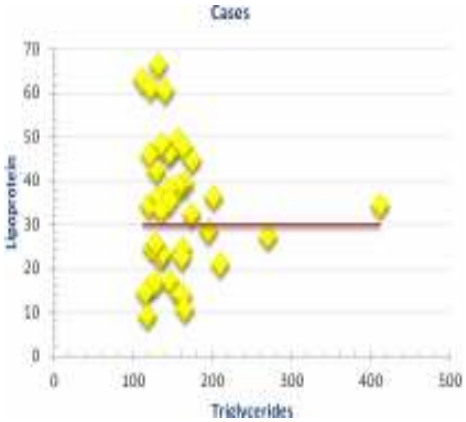


Fig 30: Correlation of Lp (a) with triglycerides in Cases

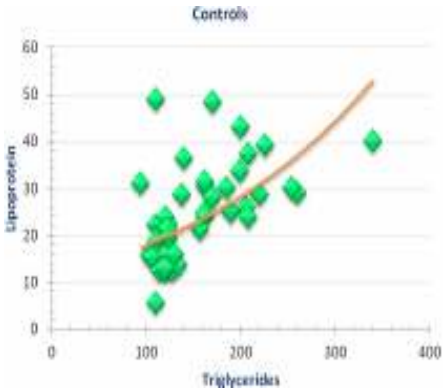


Fig 31: Correlation of Lp (a) with triglycerides in Controls

Mean Pattern of Lipoprotein (a) between different age groups

This study is performed between the cases and controls to determine the significance of age group with lipoprotein.

Table 15: Mean Pattern of Lipoprotein (a) between different age groups

Age in Years	Cases			Controls			*p* Value
	Lipoprotein (a)						
	Mean	±	SD	Mean	±	SD	
≤ 60	32.71	±	15.84	25.21	±	10.69	0.0247
> 60	37.00	±	10.78	27.40	±	5.60	0.101

Patients aged 60 years or less with ischemic brain infarct had significantly elevated lipoprotein (a) with p= 0.0247 when compared with controls. Patients older than 60 years had elevated lipoprotein (a), levels but statistically insignificant (p=0.101).

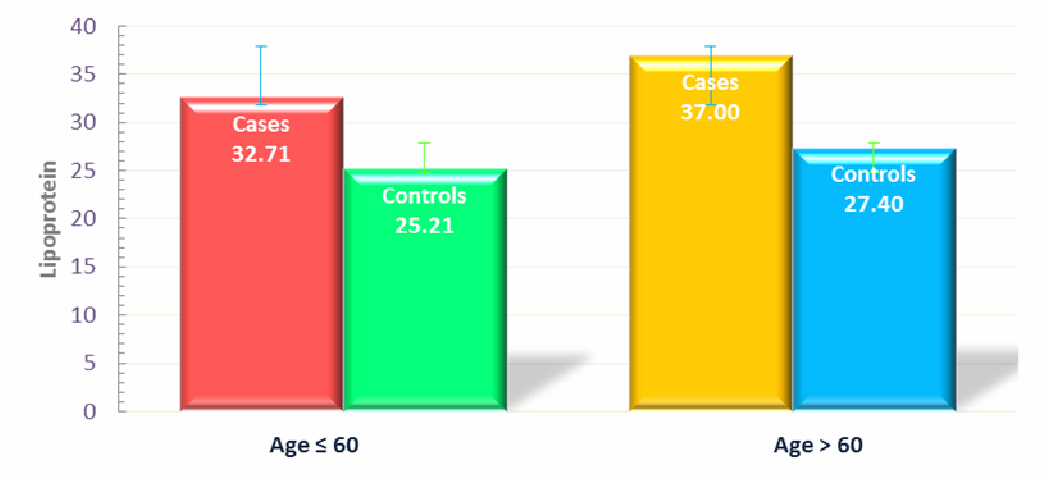


Fig 32: Distribution of Lipoprotein (a) in different age groups

Association of Risk factors with Lipoprotein (a)

This study is performed to analyze the association of risk factors with Lipoprotein(a).

Table 16: Association of Risk factors with Lipoprotein (a)

Risk Factors	Ischaemic Stroke		*p* Value
	Lipoprotein (a) mg/dl		
	0 to 30 mg/dl	> 30 mg/dl	
	No.of Cases = 17	No.of Cases = 23	
Smoking	7 (19.16)	14 (45.60)	0.469
Hypertension	5 (16.48)	12 (43.90)	0.123
Diabetes Mellitus	11 (20.14)	8 (48.05)	0.487

It is found that risk factors are not statistically significantly associated with Lipoprotein(a).

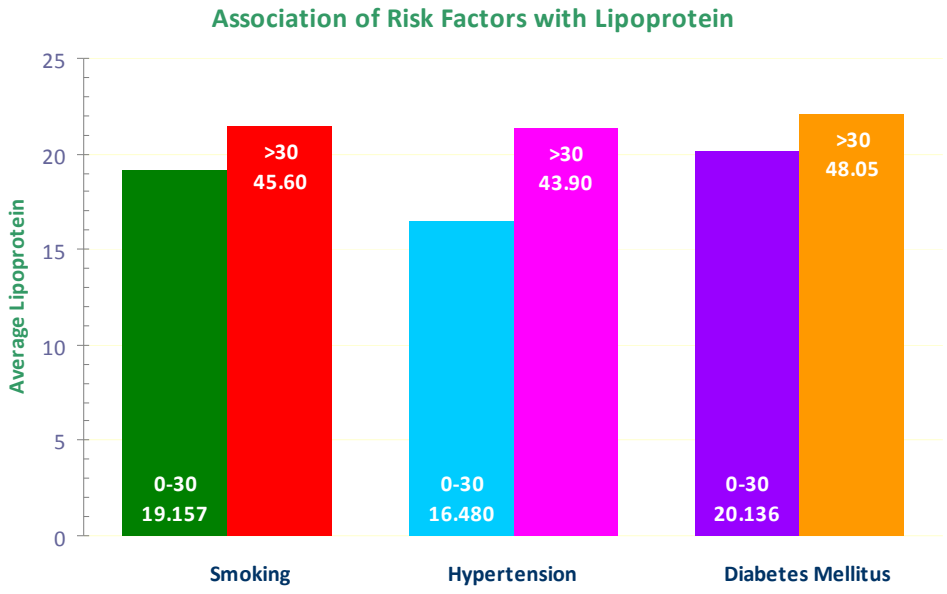


Fig 33: Association of Risk Factors with lipoprotein

Mean Pattern of Lipoprotein (a) in Normal TC and TG

This study is performed to find the significance of Total Cholesterol and Triglycerides in Ischaemic stroke patients with normal controls.

Table 17: Mean Pattern of Lipoprotein (a) in Normal TC and TG

Lipid Parameters	Lipoprotein (a)		*p* Value
	Cases	Controls	
	Mean ± SD	Mean ± SD	
Total Cholesterol (≤ 200 mg/dl)	25.55 ± 19.05	17.65 ± 12.29	0.030
Total Cholesterol (> 200 mg/dl)	40.78 ± 14.14	29.05 ± 14.92	0.190
Triglycerides (≤ 160mg/dl)	25.94 ± 21.22	13.98 ± 12.34	0.007
Triglycerides (> 160mg/dl)	29.12 ± 11.13	31.78 ± 7.08	0.422

In our study, ischaemic stroke patients with total cholesterol (≤ 200 mg/dl) and triglycerides (≤ 160mg/dl) were found to have significantly elevated lipoprotein (a) with p Values of 0.030 and 0.007 compared to matched controls.

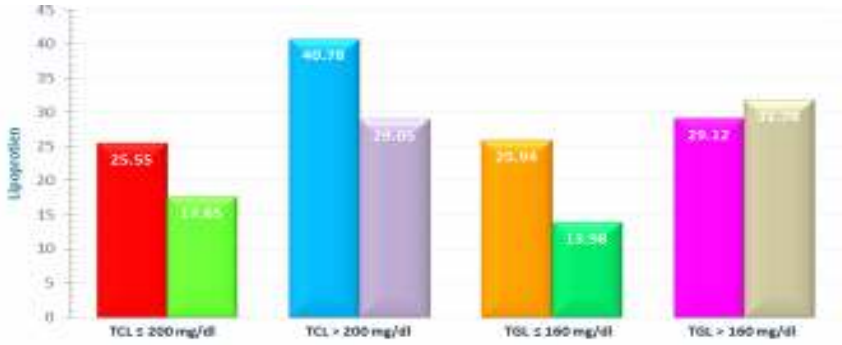


Fig 34: Mean pattern of lipoprotein in patients compared with TC and TG

DISCUSSION

The study group comprised of 40 cases of ischemic stroke patients (25 male and 15 female subjects) and 40 controls (23 male and 17 female subjects) with an average age of 52.25 ± 9.39 years in ischemic stroke group and 48.30 ± 12.06 years in control groups. Both groups were matched for age and gender.

There was no significant difference in laboratory parameters like hemoglobin, blood urea levels and serum creatinine levels between the two groups.

While comparing lipid profile of cases and controls, there was no significant difference between cases and controls. Total cholesterol, HDL cholesterol and Triglycerides were slightly reduced in cases, but LDL cholesterol was slightly elevated in cases and these values were not statistically significant. The mean lipoprotein (a) levels in the case group was 33.46±15.05 mg/dL. The mean level in the control group was 25.49±10.17. The levels were significantly higher than the control group ($p=0.007$).

Meta-analysis of data from about 31 studies, consisting of 56010 patients with > 4609 stroke patients, in order to define the

possible association of Lp(a) and stroke revealed that Lp(a) is a risk factor for cerebrovascular disease.[99]

Our study also correlated well with Jurgans G, Koltringer P[84] The Framingham heart study showed that elevated plasma Lipoprotein (a) was an independent predictor of stroke.[100]

In our study, patients aged less than or equal to 60 years had significantly raised Lipoprotein(a) levels ($p=0.0247$). Patients aged more than 60 years had elevated Lp(a) levels though this was not statistically significant ($p=0.101$).

Nagayama et al had reported higher lipoprotein levels in patients aged less than 45 years.[84]

In a study conducted by the department of Medicine at Lady Hardinge medical college, New Delhi, it was found that serum lipoprotein levels in stroke cases were elevated ($p< 0.001$, OR 8.2). A positive correlation was observed between homocysteine and Lp(a) levels ($r=0.75$, $p<0.001$).[101]

Lipoprotein(a) levels have been found to be genetically determined and influenced by apoliprotein gene on 6q 26-27. There is a locus on chromosome 12p.13 and was associated with the increased risk of stroke.[102] In our study, stroke patients are about three times more likely to have raised lipoprotein (a) >30/dl. HDL Cholesterol

levels were slightly increased in control group but these were not statistically significant in comparison to the study group. The total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride levels was reduced in the case group in comparison to the control group, but the difference was not statistically significant. We found no or trivial correlation between lipid parameters and the study group. However a correlation was observed between Lp (a) and triglyceride levels in the control group (r=0.521).

Similar to our study, studies conducted by Handan Misirli and colleagues.[103] found no significant correlation between various lipid parameters .HDL levels were not found to correlate with the risk of ischemic stroke in our study. This pattern of correlation was also observed by Gordon et al.[99]

Our study reinforced the findings of earlier studies that found no significant correlation between LDL Serum cholesterol and the risk of stroke.[104]

In our study, patients with total cholesterol levels (<200 mg %) and normal total triglyceride levels (<160 mg%) had high Lp(a) levels which was found to be of statistical significance (p=0.030, p=0.007 respectively) compared to that of controls.

Diabetes mellitus was found in 19 subjects (47.5%) of the cases and 12 subjects (30%) among controls. Hypertension was found in 17 subjects (42.5 %) of the cases and 11 subjects (27.5 %) among controls. Smoking was found in 21 individuals (52.5%) among cases and 16 persons (40.0%) of the control groups. The risk factors were increased in cases when compared to controls but this increase is not statistically significant($p>0.05$ for all risk factors). Our study population is from those admitted in our ward may be the representative of general population, so it is very unlikely to have selection bias.

Thus, the results of this study prove that lipoprotein (a) has intense effect on ischemic stroke patients.

SUMMARY

The study group consisted of total 80 subjects, 40 in the case group and 40 in the control group. Average age in cases group was 52.25±9.39 years and in control group was 48.30±12.06 years. They were matched for age and gender.

Serum lipid profile and lipoprotein (a) of 40 ischaemic stroke patients was studied and compared with those of the age and gender matched controls.

The mean value of lipoprotein (a) was significantly higher in the study group (33.46±15.05 mg/dL) when compared to the controls (25.49±10.17 mg/dL) with p=0.007 and also patients aged <60years had significantly elevated Lp(a) levels p=0.0247.

The proportion of elevated lipoprotein (a) > 30 mg/dL was also significantly increased in cases when compared to the control group. Ischaemic stroke patients were 2.81 times more likely to have elevated lipoprotein (a) >30mg/dl with p=0.025.

Ischaemic cerebrovascular disease patients with normal cholesterol levels (<200mg/dl) and normal triglyceride levels

(<160mg/dl) were found to have significantly raised Lp(a) compared to controls.

The effect of hypertension, diabetes mellitus and smoking on lipoprotein (a) was studied and found to have no statistical significance. Serum lipids did not show statistical significance in study group when compared to the controls.

CONCLUSION

- Ischemic stroke patients had higher levels of Lipoprotein (a). These were significant in comparison to the age and gender matched controls.
- An elevated lipoprotein (a) level is an independent risk factor for ischaemic stroke, in individuals less than or equal to 60 years.
- Ischemic Cerebro Vascular Disease patients with cholesterol levels <200 mg/dL and triglycerides level <160 mg/dL had significantly elevated lipoprotein (a) levels compared to controls.
- This case-control study showed that the association of plasma lipid concentration with ischemic stroke was not statistically significant.
- Cerebrovascular disease being the third most common cause for mortality, modification of Lp(a) levels at an early stage can be aimed at to reduce the overall risk of stroke and to prevent its occurrence in the future.

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PROFORMA

Name : Age : Sex :

Address : IP Number :

Chief Complaints :

Diabetes : Duration : Hypertension : Duration :

Treatment : Treatment :

Past History :

Family History :

Personal History :

- Smoking
- Alcohol
- Others

Menstrual History :

Treatment History :

General Examination :

Pulse Rate : Blood Pressure :

Respiratory rate : Temperature :

System Examination :

- CVS
- RS
- P/A
- CNS
    - Higher Mental Function
    - Speech :
    - Cranial Nerves :
    - Motor System :
        - Bulk
        - Tone
        - Power
        - Reflex DTR

          Plantar response
    - Cerebellam
    - Extra pyramidal system

Investigations :

- Complete Haemogram
- Fasting Blood Sugar (FBS): (mg/dl)
- Post prandial Blood sugar (PPBS): (mg/dl)
- Blood Urea (mg/dl)
- Serum Creatinine (mg/dl)
- Total Cholesterol (TC) (mg/dl)
- Triglyceride (TG) (mg/dl)
- High-density lipoprotein (HDL) (mg/dl)
- Low-density lipoprotein (LDL) (mg/dl)
- Very low-density lipoprotein (VLDL) (mg/dl)
- Lipoprotein (a) (mg/dl)
- Electro Cardiogram (ECG)
- Echocardiogram (ECHO)
- CT Scan

MASTER CHART - CASES

Sl. No	Name	Age	Sex	IP Number	DM	HTN	Smoking	Hb	Urea	S.Creatinine	ECG	ECHO	CT Scan	TC	LDL	HDL	VLDL	TG	LP (a)
1	Jeyamurugan	51	M	35796	N	N	Y	15.9	31	1.1	WNL	WNL	Infract	212	139	40	33	166	39
2	Purushothaman	40	M	43946	Y	N	Y	14.2	22	0.6	WNL	WNL	Infract	185	121	39	25	124	24.3
3	Dhanapal	30	M	17017	N	Y	Y	16.3	42	1.2	WNL	WNL	Infract	183	141	20	22	112	62.9
4	Thankaraj	60	M	12209	Y	N	Y	11.5	65	1.2	WNL	WNL	Infract	161	87	45	29	146	46
5	Rathinam	55	M	49287	N	Y	Y	11	40	1	WNL	WNL	Infract	198	142	24	32	160	38.3
6	Palaniammal	65	F	15928	Y	Y	N	16	29	1.2	WNL	WNL	Infract	190	138	28	24	122	15.4
7	Palani	48	M	48082	N	N	Y	10.2	27	0.8	WNL	WNL	Infract	194	68	44	82	412	34
8	Adbul Basha	67	M	5195	N	Y	N	9.9	38	1	WNL	WNL	Infract	186	99	47	40	202	36
9	Rajendran	55	M	49354	N	Y	Y	10.3	48	0.8	WNL	WNL	Infract	166	98	33	35	174	32
10	Lakshmi	51	F	18068	Y	Y	N	8	32	0.6	WNL	WNL	Infract	172	105	35	32	158	13.8
11	Pachamutthu	55	M	18105	Y	Y	Y	13.2	26	1.6	WNL	WNL	Infract	164	99	39	26	132	66
12	Radha	48	F	32167	N	Y	Y	18	27	0.9	WNL	WNL	Infract	186	119	40	27	135	22.3
13	Jothy	42	F	24481	Y	N	N	9.8	24	0.8	WNL	WNL	Infract	158	89	36	33	163	24.2
14	Murugasen	45	M	47362	N	N	Y	12	26	0.9	WNL	WNL	Infract	226	182	20	24	122	60.9
15	Subramani	65	M	43931	N	Y	Y	11.3	27	0.7	WNL	WNL	Infract	174	105	40	29	146	46
16	Chellayi	49	F	29106	Y	N	N	11.3	28	1.9	WNL	WNL	Infract	190	123	39	28	138	23
17	Nadasen	43	M	19320	N	N	Y	8	23	1.4	WNL	WNL	Infract	164	103	35	26	129	16.3
18	Pappu	60	F	32473	Y	Y	N	11.1	32	1.5	WNL	WNL	Infract	152	87	37	28	141	60.2
19	Alamelu	45	F	33448	N	N	N	15.2	49	1	WNL	WNL	Infract	186	118	33	35	175	44.3
20	Kandhan	60	M	46209	Y	N	N	6.9	50	1.2	WNL	WNL	Infract	149	79	38	32	162	22.2
21	Chenniayapan	45	M	44048	Y	N	Y	9.3	38	1.8	WNL	WNL	Infract	168	102	39	27	136	48
22	Kaliyappan	57	M	16905	Y	N	Y	13	34	1.2	WNL	WNL	Infract	206	126	41	39	195	28.2
23	Sampoornam	55	F	34271	Y	N	N	12	44	0.9	WNL	WNL	Infract	187	125	39	23	116	14.3

24	Ponnamal	62	F	34896	Y	N	N	16	34	1.2	WNL	WNL	Infract	168	103	34	31	157	38.6
25	Ponnuswamy	55	M	43990	N	N	Y	11	65	0.8	WNL	WNL	Infract	179	109	37	33	163	13.5
26	Gowri	60	F	49604	Y	Y	N	12.4	36	1.1	WNL	WNL	Infract	191	123	35	33	166	10.3
27	Indrani	44	F	49776	N	N	N	12.3	36	1.1	WNL	WNL	Infract	164	96	39	29	146	16.8
28	Kanakaraj	59	M	48238	N	N	Y	10.3	36	2.1	WNL	WNL	Infract	178	114	40	24	118	8.9
29	Murugan	48	M	13244	N	N	Y	10	42	0.9	WNL	WNL	Infract	192	128	40	24	120	34
30	Palaniammal	65	F	15928	Y	Y	N	12.7	47	1.7	WNL	WNL	Infract	158	90	39	29	146	38
31	Lakshmi	52	F	18068	Y	N	N	12.3	44	0.6	WNL	WNL	Infract	168	101	41	26	130	42
32	Lakshmanan	65	M	34377	N	N	Y	9	30	1.3	WNL	WNL	Infract	159	82	46	31	156	49
33	Venkattamal	67	F	38204	N	Y	N	11.2	46	1.1	WNL	WNL	Infract	164	99	39	26	132	36
34	Veeramal	55	F	41681	Y	N	N	10.1	48	1.4	WNL	WNL	Infract	189	121	42	26	129	25.2
35	Ramanathan	33	M	18099	Y	Y	N	10.3	70	1.6	WNL	WNL	Infract	162	100	38	24	121	45.6
36	Kasi	42	M	38079	Y	Y	Y	10	32	1.3	WNL	WNL	Infract	176	114	20	42	210	20.6
37	Perumal	55	M	43710	N	Y	Y	10	70	0.9	WNL	WNL	Infract	203	128	46	29	147	35
38	Gopal	55	M	11279	N	N	N	8.9	71	0.8	WNL	WNL	Infract	178	83	41	54	270	27
39	Madhu	37	M	12892	N	N	Y	7.9	24	1	WNL	WNL	Infract	156	84	39	33	164	47.3
40	Ramsingh	45	M	50541	N	Y	N	13.6	43	2	WNL	WNL	Infract	178	106	45	27	136	32.9

MASTER CHART - CONTROLS

Sl. No	Name	Age	Sex	IP Number	DM	HTN	Smoking	Hb	Urea	S.Creatinine	ECG	ECHO	TC	LDL	HDL	VLDL	TG	LP (a)
1	Krishnan	48	M	36499	N	Y	Y	12.1	52	1.1	NSR	NS	158	82	39	37	185	30
2	Mani	27	M	36469	N	N	Y	10.6	36	0.7	NSR	NS	196	129	42	25	127	12.3
3	Gopal	37	M	36480	Y	N	N	11.6	34	0.9	NSR	NS	149	86	38	25	124	15.9
4	Subramani	56	M	36489	N	N	N	8	26	1.1	NSR	NS	185	117	41	27	134	13.6
5	Palaniswamy	44	M	36542	N	Y	Y	11	42	1.2	NSR	NS	151	74	39	38	190	24.9
6	Chinnathalan	58	M	45102	N	N	Y	8	29	0.7	NSR	NS	160	85	35	40	199	33.5
7	Krishnan	65	M	13230	Y	N	Y	9.6	29	0.9	NSR	NS	138	82	34	22	110	22.1
8	Rajan	55	M	13429	Y	Y	N	10.6	40	1.2	NSR	NS	142	82	38	22	111	18.6
9	Rajendran	47	M	14907	N	N	Y	13.6	33	1.2	NSR	NS	202	142	38	22	110	48.9
10	Senthilrajan	37	M	19150	N	N	N	15.2	39	0.8	NSR	NS	142	62	36	44	220	28.6
11	Mary	40	F	50645	N	Y	N	11.6	20	0.9	NSR	NS	233	175	35	23	115	12.3
12	Sagunthala	51	F	50667	Y	Y	N	10.3	36	1.1	NSR	NS	136	78	35	23	117	22.3
13	Yasodha	47	F	51633	N	N	N	8	18	0.8	NSR	NS	210	144	44	22	110	5.6
14	Lakshmi	50	F	52920	Y	N	N	13	38	1.3	NSR	NS	179	109	37	33	163	30.2
15	Kamatchi	40	F	52890	N	N	N	9.8	40	0.7	NSR	NS	116	61	30	25	124	22.3
16	Alamelu	55	F	29042	Y	N	N	8.2	32	0.9	NSR	NS	160	97	39	24	120	12.3
17	Kamala	40	F	30607	N	N	N	10.9	63	1	NSR	NS	174	100	42	32	162	24.8
18	Ramanbee	60	F	34417	N	Y	N	6.9	89	1.6	NSR	NS	212	137	35	40	200	43
19	Lalitha	65	F	36991	Y	N	N	10.9	48	0.7	NSR	NS	164	73	39	52	260	29
20	Velliyammal	50	F	36944	N	N	N	13.6	28	0.7	NSR	NS	164	82	40	42	208	37.3
21	Kunjammal	58	F	39329	N	N	N	14.2	29	1.1	NSR	NS	152	83	37	32	162	24

22	Anthoniyamma	40	F	39420	N	N	N	12.3	36	1.1	NSR	NS	152	63	38	51	254	30.1
23	Unnamalai	60	F	45120	Y	N	N	8	31	0.6	NSR	NS	210	126	39	45	226	39.2
24	Karupayee	68	F	47354	N	Y	N	11	32	0.9	NSR	NS	148	86	38	24	121	23.8
25	Gopal	57	M	38205	N	N	Y	13	28	1.1	NSR	NS	218	113	37	68	340	40.1
26	Subramani	56	M	38230	N	Y	Y	12.4	22	0.7	NSR	NS	256	192	39	25	123	21.3
27	Vellaiyan	60	M	38770	Y	N	N	14.6	29.8	0.8	NSR	NS	174	101	41	32	162	31.4
28	Ponnuswamy	60	M	40594	Y	N	Y	11	54	1.6	NSR	NS	206	144	43	19	94	31
29	Perumal	64	M	41743	N	Y	Y	11.6	62	1.3	NSR	NS	196	111	44	41	206	25.8
30	Balan	40	M	42902	N	N	Y	13	22	1	NSR	NS	182	118	39	25	124	19.3
31	Sithan	61	M	42976	N	N	N	9.8	26	0.9	NSR	NS	166	88	50	28	140	36.3
32	Periyaswamy	35	M	44043	N	Y	Y	7	64	1	NSR	NS	190	125	41	24	121	12.9
33	Chennakumar	25	M	45099	N	N	Y	12.6	23.8	0.8	NSR	NS	169	84	43	42	208	23.9
34	Soundarrajan	23	M	45123	N	N	Y	13	49	2.1	NSR	NS	206	134	38	34	170	48.3
35	Muthu	50	M	46149	Y	N	Y	10.4	28	0.9	NSR	NS	215	135	46	34	170	28
36	Kondappanayakkan	57	M	49378	Y	N	N	13.3	70	1.2	NSR	NS	198	127	43	28	138	28.6
37	Ganesan	37	M	49405	N	N	Y	12	44	0.6	NSR	NS	213	163	29	21	104	15.6
38	Chinnapillai	45	F	54203	N	Y	N	11.4	72	1.8	NSR	NS	164	93	40	31	157	21.2
39	Thenmozhi	25	F	44537	N	N	N	12.6	23	0.9	NSR	NS	184	111	47	26	130	15.8
40	Revathy	39	F	44486	N	N	N	10.4	32	1.1	NSR	NS	217	155	41	21	106	15.3

LEGEND TO MASTER CHART

CT	Computed Tomography
DM	Diabetes Mellitus
ECG	Electrocardiogram
ECHO	Echocardiogram
Hb	Hemoglobin
HDL	High Density lipoprotein
HTN	Hypertension
LDL	Low Density Lipoprotein
Lp (a)	Lipoprotein a
NS	Normal Study
TC	Total Cholesterol
TG	Triglyceride
VLDL	Very Low Density Lipoprotein
WNL	Within Normal Limits
Y	Yes
N	No